to SARS-CoV-2 virus among young SOT recipients. It is still unknown if the demonstration of serologic response against the virus correlates with protection from disease in the event of future exposure to the virus. Further research is needed to examine the effectiveness of these antibodies in neutralization-based assays, as well as their clinical protection, magnitude and durability over the course of time.

This study has several limitations. Due to its retrospective nature, PCR testing was not done at uniform time points, thus potentially influencing the shedding time. However, patients were tested frequently due to our follow-up protocol for transplant recipients. Another limitation is the relatively small sample size, which is a result of the small population of pediatric SOT recipients.

In conclusion, the majority of pediatric SOT recipients who had COVID-19 in our study developed a mild disease but mounted a positive IgG response. Nevertheless, kidney transplant recipients with additional comorbidities developed a severe disease, emphasizing the need for close monitoring in this particular population.

REFERENCES

1. Doná D, Torres Canizales J, Benetti E, et al; ERN TransplantChild. Pediatric transplantation in Europe during the COVID-19 pandemic: early impact on activity and healthcare. *Clin Transplant.* 2020;34:e14063.
2. Downes KJ, Danziger-Isakov LA, Cousino MK, et al. Return to school for pediatric solid organ transplant recipients in the United States during the coronavirus disease 2019 pandemic: expert opinion on key considerations and best practices. *J Pediatric Infect Dis Soc.* 2020;9:551–563.
3. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Clinical Spectrum of SARS-CoV-2 Infection. National Institute of Health. Available at: https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/. Accessed May 1, 2021.
4. Indenbaum V, Koren R, Katz-Likvornik S, et al. Testing IgG antibodies against the RBD of SARS-CoV-2 is sufficient and necessary for COVID-19 diagnosis. *PLoS One.* 2020;15:e0241164.
5. Israel Ministry of Health. COVID-19 recovery. 2020. Available at: https://www.gov.il/en/departments/general/corona-recovered-patients. Accessed April 24, 2021.
6. Varnell C Jr, Harshman LA, Smith L, et al. COVID-19 in pediatric kidney transplantation: The Improving Renal Outcomes Collaborative [published online ahead of print January 16, 2021]. *Am J Transplant*. doi: 10.1111/ajt.16501.
7. Goss MB, Galván NTN, Ruan W, et al. The pediatric solid organ transplant experience with COVID-19: an initial multi-center, multi-organ case series. *Pediatr Transplant.* 2021;25:e13868.
8. Zachariah P, Johnson CL, Halabi KC, et al; Columbia Pediatric COVID-19 Management Group. Epidemiology, clinical features, and disease severity in patients with coronavirus disease 2019 (COVID-19) in a children's hospital in New York City, New York. *JAMA Pediatr.* 2020;174:e202430.
9. Han MS, Choi EH, Chang SH, et al. Clinical characteristics and viral RNA detection in children with coronavirus disease 2019 in the Republic of Korea. *JAMA Pediatr.* 2021;175:73–80.
10. Vena A, Taramasso L, Di Biagio A, et al. Prevalence and clinical significance of persistent viral shedding in hospitalized adult patients with SARS-CoV-2 infection: a prospective observational study. *Infect Dis Ther.* 2021;10:387–398.

ANTIBODIES TO SEASONAL CORONAVIRUSES RARELY CROSS-REACT WITH SARS-COV-2

FINDINGS FROM AN AFRICAN BIRTH COHORT

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Abstract: Antibodies to seasonal human-coronaviruses (sHCoV) may cross-protect against SARS-CoV-2. We investigated antibody responses in biobanked serum obtained before the pandemic from infants with polymerase chain reaction-confirmed sHCoV. Among 141 samples with antibodies to sHCoV, 4 (2.8%) were positive for SARS-CoV-2-S1 and 8 (5.7%) for SARS-CoV-2-S2. Antibodies to sHCoV rarely cross-react with SARS-CoV-2 antigens and are unlikely to account for mild pediatric illness.

Key Words: seasonal coronavirus, cross-protection, antibodies, child, COVID-19

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Children have been largely spared in the COVID-19 pandemic, developing predominantly asymptomatic or mild disease.[1] Globally, children constitute around 8% of infections, <2% of hospitalizations and <1% of all COVID-19 associated mortality in high and low-middle income countries (LMICs).[2] In South Africa, 9% of infections and <0.1% of COVID deaths occur in children or adolescents, who comprise >30% of the population.[3] Although pneumonia remains a major cause of mortality and morbidity in children in LMICs, risk factors for severe pneumonia such as malnutrition, HIV or prematurity have also not emerged as risk factors for COVID-19.[4]

A key knowledge gap is why pediatric disease is relatively mild. One hypothesis is that cross-protection to SARS-CoV-2 may occur from immunity to one of the 4 seasonal coronaviruses [seasonal human-coronaviruses (sHCoVs); 229E, NL63, OC43 and HKU1], which are common and circulate seasonally worldwide.[5–9] Recently, individuals, including children, unexposed to SARS-CoV-2, were reported to have antibodies to the S2 subunit of SARS-CoV-2 spike (S) protein from presumed prior sHCoV infection.[7] Shared sequence conservation between sHCoVs and SARS-CoV-2 raises the possibility that immunity against sHCoV may cross-protect against SARS-CoV-2.

We recently reported the epidemiology of sHCoV infection in infants preceding the COVID-19 pandemic in an African birth cohort, the Drakenstein Child Health study (DCHS).[10] By leveraging this unique dataset and matching biobank of samples, we investigated cross-reactivity of antibodies induced by PCR-confirmed sHCoV infection prior to the COVID pandemic against SARS-CoV-2.

METHODS

We investigated serologic responses to sHCoVs and to SARS-CoV-2 spike (S) antigen in biobanked samples collected before the pandemic. Samples were collected from infants with polymerase chain reaction (PCR)-confirmed sHCoV and age-matched controls without documented sHCoV. Infants enrolled in the DCHS, a birth cohort study in a low-income community, followed infants from birth at 6, 10, 14 weeks and 6, 9 and 12 months, during which serum was collected and biobanked.[11] Intensive follow-up was done, in a subset who chose to participate, comprising fortnightly nasopharyngeal sample collection through the first year of life. Active surveillance for pneumonia, using WHO case definitions, was done. At each pneumonia episode, a nasopharyngeal swab and a serum sample were taken; convalescent serum was also obtained 4–6 weeks after pneumonia.

Nasopharyngeal swabs from the time of pneumonia and 2 weekly up to 90 days before pneumonia were tested with qPCR to detect sHCoV -229E, -NL63, -OC43 and -HKU1, as previously described.[12] Swabs from age-matched control children without pneumonia in the cohort were also tested over the equivalent period.

The study was approved by the Human Research Ethics Committee, Faculty of Health Sciences University of Cape Town. Mothers provided written informed consent.

Microbiologic Testing

Nasopharyngeal swabs preserved in PrimeStore nucleic acid preservation medium (Longhorn Vaccines and Diagnostics, San Antonio, TX), transported on ice and frozen at –80 °C for batch testing. Swabs underwent mechanical lysis on a Tissuelyzer LT (Qiagen, Hilden, Germany) followed by total nucleic acid extraction (QIAsymphony Virus/Bacteria Mini Kit, Qiagen, Hilden, Germany). Quantitative, multiplex, real-time PCR (qPCR) with FTDResp33 (Fast-Track Diagnostics, Esch-sur-Alzet, Luxembourg) identified potential respiratory pathogens including sHCoV (-NL63, -229E, -OC43 and -HKU1). Standard curves were derived using standards supplied by the manufacturer.

Antibody Measurements

Biobanked serum samples matched to sHCoV-tested nasopharyngeal samples collected at the time of pneumonia were tested for antibodies. In addition, matched convalescent samples taken 4–6 weeks after a pneumonia episode were also tested, when available. Serum was aliquoted, and frozen until batch shipping to the WHO International Reference laboratory for Pneumococcal Serology at University College London where samples were tested for IgG to each of the 4 sHCoVs. Samples were also analyzed in a multiplexed assay of IgG to SARS-CoV-2 of S1 and S2 and trimeric spike antigen (MSD SARS-Coronavirus Plate 1, Rockville, MD) as described, as spike provides the greatest sensitivity and specificity for SARS-CoV-2.[13]

Analysis

Data were analyzed using STATA 14.1 (STATA Corporation, College Station, TX) and GraphPad Prism version 9.0.2 (GraphPad, San Diego, CA). Data were summarized as frequencies (percent) if categorical and median [interquartile range (IQR))] if continuous. Wilcoxon rank-sum test (Mann–Whitney *U* test), Kruskal–Wallis test and χ^2 or Fisher's exact test were used for crude comparisons, as appropriate. The antibody titers for sHCoV, CoV-2-S and CoV-2-S2 were reported as geometric means [95% confidence interval (CI)].

RESULTS

We identified 42 pneumonia cases positive for sHCoV from whom serum was available at the time of episode with 33 matched convalescent serum samples at 4–6 weeks after pneumonia, all collected pre-COVID. These were matched to 39 pneumonia cases negative for sHCoV, but with other identified organisms. We also included identified 16 samples from children who were asymptomatic but had sHCoV detected (with matched serum available), and matched these to 21 samples from asymptomatic children without sHCoV. In total, there were 151 biobanked serum samples available from 114 children [median age 6 (3.1–7.3) months]. Four children had more than one episode of pneumonia; the median (IQR) time between pneumonia episodes was 141 (96–186) days, so each episode was included as an independent episode. Children with sHCoV-associated pneumonia were younger than those with asymptomatic sHCoV infection (median age 4.6 vs. 6 months, $P = 0.010$) (see Table, Supplemental Digital Content 1, http://links.lww.com/INF/E523). OC43 was the commonest sHCoV, occurring in 29 (24.6%), followed by NL63 (14, 11.9%), HKU1 (12, 10.2%) and 229E (4, 3.4%).

Geometric mean (95% CI) IgG antibody titers for each sHCoV were higher in those who were PCR-positive (at the same time point) for the corresponding sHCoV compared with those who were negative (Table 1). GMTs were similar in sHCoV pneumonia cases compared with asymptomatic sHCoV-positive controls [24.61 (14.40–42.06) vs. 33.49 (14.78–75.90) for OC43, $P = 0.402$; 62.84 (34.43–114.67) vs. 42.19 (17.29–102.99) for NL63, $P = 0.396$; 25.64 (14.87–44.21) vs. 26.77 (9.52–75.26), $P = 0.972$ for HKU1; 18.44 (11.32–30.03) vs. 8.80 (5.20–14.88) for 229E, $P = 0.098$] (Figure, Supplemental Digital Content 2, http://links.lww.com/INF/E524). Among children with sHCoV-associated pneumonia, there was an increase in GMTs in matched pneumonia and convalescent sera [31.88 (10.76–94.42) vs. 113.95 (37.67–344.74) for OC43; $P = 0.098$; 60.50 (13.02–281.18) vs. 194.57 (89.16–424.60) for NL63, $P = 0.252$; 13.70 (4.13–45.48) vs. 90.71 (29.36–280.27), $P = 0.024$ for HKU1; 61.35 (10.18–369.74) vs. 267.87 (10.43–6876.75) for 229E, $P = 0.248$] (Figure, Supplemental Digital Content 3, http://links.lww.com/INF/E525).

Antibodies were specific to each sHCoV, with no cross-reactivity across each of the 4 sHCoVs (Table 1). There was no clear pattern of cross-reactivity for SARS-CoV-2-S1 or S2, by the presence of any sHCoV (Table 1). Among 141 samples above the lower limit of detection for antibodies to a sHCoV, only 4 (2.84%) were positive for SARS-CoV-2-S1, while 8 (5.7%) were weakly positive for SARS-CoV-2-S2 (3 of which were also positive to SARS-CoV-2-S1).

DISCUSSION

This study, using samples collected preceding the COVID-19 pandemic, found that antibody responses to documented sHCoV infection or disease are robust and specific for each sHCoV in infants in an African birth cohort. While antibody levels did not differ between infants who had symptomatic compared with asymptomatic infection, titers increased in convalescence, following pneumonia. However, little cross-reactivity against SARS-CoV-2, occurred, indicating that antibodies to sHCoV are unlikely to cross-protect against COVID-19. The data on lack of cross-reactivity between different sHCoV also support our previous finding that infection with different sHCoV occurs within short intervals of each other.[10]

Several explanations have been proposed for lower rates of infection and mild disease from SARS-CoV-2 globally in children. These include testing practices with lower case ascertainment due to asymptomatic or mild disease,[1] lower expression of angiotensin-converting-enzyme-2 viral receptor in pediatric compared with adult airway epithelial cells,[14] more robust innate immune responses in children[8] or induction of trained immunity following BCG immunization or infection,[15] that protects against

TABLE 1. Antibody Titers in Children by PCR-positive sHCoV and Cross-reactivity to SARS-CoV-S (S1, S2)

	229E PCR			OC43 PCR			HKU1 PCR			NL63 PCR		
	Positive, n = 4	Negative, n = 114	*P*	Positive, n = 29	Negative, n = 89	*P*	Positive, n = 12	Negative, n = 106	*P*	Positive, n = 14	Negative, n = 104	*P*
229E IgG	**61.35 (10.18–369.74)**	**14.40 (11.09–18.71)**	**0.026**	14.68 (8.11–26.58)	15.28 (11.42–20.44)	0.645	8.91 (5.94–13.36)	16.06 (12.09–21.34)	0.277	15.29 (5.93–39.40)	15.11 (11.51–19.83)	0.724
OC43 IgG	13.57 (1.98–93.05)	24.21 (17.92–32.71)	0.550	**56.24 (29.90–105.76)**	**17.93 (13.08–24.57)**	**0.001**	14.60 (5.69–37.48)	25.08 (18.36–3427)	0.233	14.69 (5.77–37.40)	25.33 (18.54–34.60)	0.181
HKU1 IgG	13.32 (1.64–108.38)	23.39 (17.16–31.89)	0.549	30.77 (15.17–62.41)	20.86 (14.93–29.13)	0.331	**44.25 (12.42–157.63)**	**21.31 (15.63–29.04)**	**0.208**	17.11 (6.60–44.35)	23.87 (1728–32.99)	0.395
NL63 IgG	176.67 (24.55–1271.48)	54.66 (38.78–77.05)	0.173	33.11 (15.95–68.76)	67.85 (46.53–98.94)	0.054	55.00 (21.07–143.57)	57.10 (39.74–82.03)	0.936	**106.22 (34.25–329.37)**	**52.29 (36.72–74.48)**	**0.167**
SARS-CoV-2-S1 IgG	0.54 (0.54–0.54)	0.56 (0.54–0.58)	0.744	0.59 (0.52–0.67)	0.55 (0.54–0.56)	0.084	0.62 (0.47–0.81)	0.55 (0.54–0.57)	0.170	0.54 (0.54–0.54)	0.56 (0.54–0.58)	0.522
SARS-CoV-2-S2 IgG	8.16 (1.72–38.73)	11.04 (8.86–13.75)	0.583	12.41 (7.24–21.26)	10.48 (8.33–13.19)	0.667	21.85 (6.73–70.98)	10.10 (8.24–12.38)	0.078	8.44 (5.37–13.28)	11.31 (8.93–14.33)	0.489

Results are geometric means (95% CI); bolded values show comparison of antibody levels for specific sHCoV by PCR positivity for that sHCoV.

SARS-CoV-2 disease. Immunity to sHCoV with seasonal circulation, has also been hypothesized as a mechanism for protection.[5–7]

In this study, IgG antibodies to sHCoVs rarely cross-reacted with SARS-CoV-2-S including the S1 and S2 components. Our findings differ from those recently published in which IgG antibodies binding to the S2 component of SARS-CoV-2 were detected in some individuals before the pandemic, using a flow cytometry assay.[7] Differences in methodology, populations sampled or interpretation of findings may explain such differences. Only some individuals were reported to have cross-reactivity on flow cytometry (eg, only 5 of 34 subjects with confirmed sHCoV infection), compared with our findings of 8 of 114 children with cross-reactivity. Cross-reactivity was rare in healthy donor cohorts (occurring only in 16/302; 5.3%) but the highest prevalence of cross-reactivity occurred in donors 6–16 years. The strength of our study is that infants had PCR-confirmed sHCoV infection before the pandemic, and cross-reactivity was assessed both at the time of disease and 4–6 weeks after when titers increased. It is possible that cross-reactivity may occur following several infections, and therefore occur later in childhood. Furthermore, pre-existing cross-reactive cellular T-cell immune responses to SARS-CoV-2, presumably due to prior infection with sHCoV, have been demonstrated in some studies, and may provide a different mechanism for protection against SARS-CoV-2.[6,16,17]

A limitation of this study is that serologic responses to sHCoV were investigated only during the first year of life; however, this age group has the highest incidence of childhood pneumonia and respiratory infections, as previously shown.[12] Another limitation is that T-cell responses were not evaluated. Strengths are strong surveillance for pneumonia,[18] PCR confirmation of sHCoV episodes, matching antibody measurements including convalescent sera, and the inclusion of a matched control group in an LMIC population-based cohort.

In summary, while sHCoV infections were common and associated with robust antibody responses in infants, minimal cross-reactivity against SARS-CoV-2 spike antigen was detected. Antibodies to sHCoV are unlikely to provide substantial cross protection against COVID-19, but other mechanisms such as cross-reactive cellular immune responses may be important in ameliorating disease in children.

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REFERENCES

1. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr*. 2020;109:1088–1095.
2. Worldometers.info. Worldometer COVID-19 coronavirus data. Available at: https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/. Accessed June 26, 2021.
3. Monthly COVID-19 in children. National Institute Communicable Diseases (NICD), South Africa. Available at: https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/monthly-covid-19-in-children/. Accessed June 26, 2021.
4. Zar HJ, Dawa J, Fischer GB, et al. Challenges of COVID-19 in children in low- and middle-income countries. *Paediatr Respir Rev*. 2020;35:70–74.
5. Braun J, Loyal L, Frentsch M, et al. SARS-CoV-2-reactive T cells in healthy donors and patients with COVID-19. *Nature*. 2020;587:270–274.
6. Mateus J, Grifoni A, Tarke A, et al. Selective and cross-reactive SARS-CoV-2 T cell epitopes in unexposed humans. *Science*. 2020;370:89–94.
7. Ng KW, Faulkner N, Cornish GH, et al. Preexisting and de novo humoral immunity to SARS-CoV-2 in humans. *Science*. 2020;370:1339–1343.

8. Pierce CA, Preston-Hurlburt P, Dai Y, et al. Immune responses to SARS-CoV-2 infection in hospitalized pediatric and adult patients. *Sci Transl Med*. 2020;12:eabd5487.
9. Stervbo U, Rahmann S, Roch T, et al. Epitope similarity cannot explain the pre-formed T cell immunity towards structural SARS-CoV-2 proteins. *Sci Rep*. 2020;10:18995.
10. Nicol MP, MacGinty R, Workman L, et al. A longitudinal study of the epidemiology of seasonal coronaviruses in an African Birth Cohort. *J Pediatric Infect Dis Soc*. 2021;10:607–614.
11. Zar HJ, Barnett W, Myer L, et al. Investigating the early-life determinants of illness in Africa: the Drakenstein Child Health Study. *Thorax*. 2015;70:592–594.
12. Zar HJ, Barnett W, Stadler A, et al. Aetiology of childhood pneumonia in a well vaccinated South African birth cohort: a nested case-control study of the Drakenstein Child Health Study. *Lancet Respir Med*. 2016;4:463–472.
13. Johnson M, Wagstaffe HR, Gilmour KC, et al. Evaluation of a novel multiplexed assay for determining IgG levels and functional activity to SARS-CoV-2. *J Clin Virol*. 2020;130:104572.
14. Bunyavanich S, Do A, Vicencio A. Nasal gene expression of angiotensin-converting enzyme 2 in children and adults. *JAMA*. 2020;323:2427–2429.
15. Netea MG, Giamarellos-Bourboulis EJ, Domínguez-Andrés J, et al. Trained immunity: a tool for reducing susceptibility to and the severity of SARS-CoV-2 infection. *Cell*. 2020;181:969–977.
16. Grifoni A, Weiskopf D, Ramirez SI, et al. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. *Cell*. 2020;181:1489–1501.e15.
17. Woldemeskel BA, Kwaa AK, Garliss CC, et al. Healthy donor T cell responses to common cold coronaviruses and SARS-CoV-2. *J Clin Invest*. 2020;130:6631–6638.
18. le Roux DM, Myer L, Nicol MP, et al. Incidence of childhood pneumonia: facility-based surveillance estimate compared to measured incidence in a South African birth cohort study. *BMJ Open*. 2015;5:e009111.

ANTIBIOTIC THERAPY OF AN INFANT WITH A *BREVIBACTERIUM CASEI* VENTRICULOPERITONEAL SHUNT INFECTION

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Abstract: We describe a newborn infant with hydrocephalus and a ventriculoperitoneal shunt infection caused by *Brevibacterium casei*. Essential for correct diagnosis was rapid species identification by matrix-assisted laser desorption/ionization time-of-flight, after initial report of coryneform bacteria. The patient responded well to vancomycin and rifampicin for 15 days. The shunt was not removed. Repeated cerebrospinal fluid cultures up to 4 months after therapy remained negative.

Key Words: *Brevibacterium*, ventriculoperitoneal shunt, infection

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Brevibacterium species are catalase-positive, nonspore forming, immotile, aerobic Gram-positive rods, closely related to corynebacteria. They are environmental bacteria often found in dairy products but also on human skin surfaces and have been considered as nonpathogenic commensals.[1,2] However, they can cause severe infections like peritonitis, meningitis, cholangitis and sepsis, mainly in immunocompromised patients.[1] Over the last decade, *Brevibacterium* catheter-related infection are also reported,[3–6] probably related to the biofilm-forming capacity of this bacterium.[7] There is conflicting evidence whether surgical removal of the catheter is needed to clear a *Brevibacterium* catheter-related infection,[1,3–6] and no management guidelines are established. To date, we are only aware of 1 published case of a *Brevibacterium* infection in a child younger than 1 year of age, a neonate with an osteomyelitis.[8] We here describe a newborn infant with hydrocephalus and a ventriculoperitoneal (VP) shunt infection caused by *Brevibacterium casei*. We discuss current literature and conservative management of device-related *Brevibacterium* infections.

CASE REPORT

A term born infant was prenatally diagnosed with an obstructive hydrocephalus due to intrauterine germinal matrix bleeding and secondary aqueduct stenosis. A VP shunt was inserted on day 5 of life due to rapidly increasing head circumference. He had a complicated postoperative course, initially with over-drainage and rebleeding. Later there were signs of underdrainage with mild subcutaneous cerebrospinal fluid (CSF) swelling along the shunt, and valve adjustments were done. He was discharged home after 1 month in hospital. Five days after discharge, he was readmitted presenting with increasing head circumference, bulging fontanel, irritability, CSF leakage from the surgical wound. There was also a subcutaneous lesion in the neck, stretching from the VP shunt valve to a surgical incision point behind the right ear. Some days later, he also developed fever (38.9 °C). Except for the CSF leakage and irritability, there was no other focus for infection. Laboratory tests did not show any signs of a systemic infection (Table 1). Ultrasound of the brain showed no signs of ventriculitis or meningitis.

MICROBIOLOGIC INVESTIGATIONS OF CSF

By aseptic procedure, a CSF sample for cell count and culture was obtained from the fluid-filled subcutaneous lesion in the neck. This sample showed markedly increased cell count (Table 1) and CSF protein of 4.8 g/L, but the Gram stain showed no visible bacteria. However, there was pure growth of Gram-positive rods, initially characterized as coryneform bacteria and interpreted as possible skin contamination. Due to persistent symptoms, a second CSF sample was obtained from the VP shunt valve 4 days later. This CSF sample also revealed growth of Gram-positive rods, morphologically identical to the first CSF sample. Species identification was now performed by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Billerica, MA) and suggested *B. casei*. The antibiotic susceptibility pattern of both bacterial isolates obtained from the CSF was identical. Minimum inhibitory concentration (MIC) analysis using gradient strips (Liofilchem, Roseto degli Abruzzi, Italy) revealed the following values (mg/L): rifampicin 0.016, vancomycin 0.25, gentamicin 0.25, clindamycin 0.5, ciprofloxacin 0.5, cefotaxime 1.0, penicillin 1.5, chloramphenicol 4.0. There are no defined susceptibility breakpoints for *Brevibacterium* spp. We interpreted MIC values according to the suggested clinical breakpoints for *Corynebacterium* spp. in Europe (European Committee on Antimicrobial Susceptibility Testing; https://eucast.org/ast_of_bacteria).

TREATMENT, OUTCOME AND FOLLOW-UP

Following interdisciplinary discussion and a literature review, we decided to attempt intravenous antibiotic therapy with vancomycin (15 mg/kg every 8 hours) and rifampicin (10 mg/kg every 12 hours) and to leave the VP shunt system in situ. Intrathecal