Complicated Head and Neck Infections Caused by *Streptococcus constellatus* at the End of the COVID-19 Pandemic

A Case Series

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To the Editors:

Following the canceling of COVID-19 pandemic restrictions, an increased number of invasive infections caused by *Streptococcus pyogenes* and *Streptococcus pneumoniae* have been reported.[1,2] However, there is a relative paucity of data regarding the invasive infections due to other *Streptococci* species. Herein, we report a case series of complicated head and neck infections caused by *Streptococcus constellatus* at the end of the COVID-19 pandemic.

Between October 2021 and March 2022, we observed an apparent increase in the frequency of severe head and neck infections caused by *S. constellatus* in our institution. We followed up 5 consecutive cases between 6 and 15 years old in a 6-month period (Table 1).

We reviewed the database of our microbiology laboratory for *S. constellatus*-positive cultures between January 2011 and September 2021 and could not find a positive culture. Diagnosis of head and neck infections was confirmed with contrast-enhanced computed tomography or magnetic resonance imaging. All patients underwent surgical interventions in combination with long-term antibiotic therapy. Abscess and blood culture results are shown in Table 1. Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry using the VITEK MS system (Biomeriux, France) was used for bacterial identification. Antimicrobial susceptibility testing was performed using Vitek 2 AST-ST03 (Biomeriux, France) cards. All *S. constellatus* isolates were susceptible to penicillin G (minimum inhibitory concentrations ≤0.125 mcg/mL). All 5 patients recovered uneventfully.

The *Streptococcus anginosus* group (SAG) is a subgroup of viridans streptococci that consists of 3 distinct species: *S. anginosus, Streptococcus intermedius* and *S. constellatus.* These organisms are part of the normal human flora colonizing the oropharynx, gastrointestinal, and genitourinary tracts.[3]

TABLE 1. Clinical Characteristics of Patients With Head and Neck Infections Caused by *Streptococcus constellatus*

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (year)	10	6	15	15	14
Gender	Male	Female	Female	Male	Male
Underlying disease	–	Epilepsy, cerebral palsy	–	–	–
Oral hygiene/ tooth decay	Poor/–	Poor/+	Poor/+	Poor/–	Poor/+
History of preceding sinusitis	Yes	–	–	Yes	–
Clinical presentation	Fever, headache, behavioral changes, seizures	Fever, respiratory distress, neck swelling	Limited neck movements, right buccal swelling, trismus, difficulty in swallowing	Fever, headache, right periorbital swelling	Swelling, pain and tenderness in the right mandible corner
Diagnosis	Frontal sinusitis, subdural empyema	Left branchial cleft cyst abscess	Right submandibular space abscess, mandibular osteomyelitis	Right preseptal cellulitis with eyelid abscess, subdural empyema	Right facial abscess
PICU admission	Yes	Yes	–	–	–
SARS-CoV-2 RT-PCR (preoperative)	Positive, asymptomatic	Negative	Negative	Negative	Negative
White blood cell count at admission ($\times 10^3/\mu L$)	$24 \times 10^3/\mu L$ (%78 neutrophil)	$20 \times 10^3/\mu L$ (%80 neutrophil)	$18 \times 10^3/\mu L$ (%72 neutrophil)	$8.8 \times 10^3/\mu L$ (%66 neutrophil)	$19 \times 10^3/\mu L$ (%78 neutrophil)
CRP at admission (mg/L)	183	318	235	73	60
Abscess culture	*S. constellatus*	*S. constellatus*	*S. constellatus*	*S. constellatus*	*S. constellatus*
Blood culture	–	*S. constellatus, Staphylococcus epidermidis*	*S. constellatus*	–	–
Antibiotic treatment	IV ceftriaxone (100 mg/kg) and vancomycin (60 mg/kg)	IV ceftriaxone (100 mg/kg/day) and clindamycin (40 mg/kg/day)	IV ampicillin-sulbactam (200 mg/kg/day) and clindamycin (40 mg/kg/day)	IV ceftriaxone (100 mg/kg/day) and vancomycin (60 mg/kg/day)	IV clindamycin (40 mg/kg/day)
Duration of antibiotic treatment (day)	42	14	30	30	14
Surgical treatment	Neurosurgical intervention (empyema drainage 3 times)	Otolaryngological intervention (abscess drainage)	Otolaryngological intervention (abscess drainage)	Otolaryngological, oculoplastic, and neurosurgical interventions (abscess and empyema drainage 3 times)	Otolaryngological intervention (abscess drainage)
Length of hospital stay (day)	42	21	30	30	14

CRP indicates C-reactive protein; IV, intravenous; PICU, pediatric intensive care unit; RT-PCR, real-time polymerase chain reaction.

The authors have no conflicts of interest to disclose.

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The Centers for Disease Control and Prevention recently reported an increase in pediatric streptococcal intracranial infections following the onset of the COVID-19 pandemic.[4] The SAG organisms have been increasingly reported in children with sinogenic and otogenic intracranial infections in recent years.[3] The reasons for this increase are unclear. The widespread use of pneumococcal conjugate vaccines has changed the microbial etiology of complicated sinusitis.[3] Additionally, the application of more modern microbiological techniques such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry or next-generation sequencing has increased the identification of SAG species. Lastly, the temporal association between COVID-19 pandemic and an increased number of complicated head and neck infections at our institution suggests that there may be a relationship. Speculative mechanisms of SARS-CoV-2 predisposing to complicated head and infections include (1) disruption of the respiratory microbiota and (2) alteration of the respiratory tract and oropharyngeal bacterial flora due to masking and social distancing. Prolonged use of face masks can lead to oral health problems, which are being termed "mask mouth syndrome," including bad breath, dry mouth, gingivitis, and eventually tooth decay.[5] In our case series, all 5 patients had poor oral hygiene and 2 patients had tooth decay. Since there is a known association between *S. constellatus* and dental plaque and periodontal diseases, this mechanism may be one of the reasons in our cases. Further studies are necessary to understand the reasons of the increased incidence or mechanisms of the *S. constellatus* infections.

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One-year Longitudinal Study of Antibody Profiles in Children

MIS-C Versus Children With Uncomplicated COVID-19

To the Editors:

In the spring of 2020, most children presented with an asymptomatic or paucisymptomatic infection to SARS-CoV-2,[1] while a subset of children developed a multisystem inflammatory syndrome (MIS-C). The physiopathology of MIS-C has been widely studied, but the exact cause leading to MIS-C development in some children is still unclear. We have shown previously that 1-month postinfection, the neutralizing activity of circulating antibodies and the level of serum IgA against SARS-CoV-2 were higher in MIS-C patients compared with children with uncomplicated COVID-19.[2] In contrast, no difference was observed in the levels of IgG and IgM antibodies. Here, we assessed whether the specific features of the antibody response of MIS-C children were sustained throughout a year after infection.

The MIS-C children had blood sampling at 1-month (first day of hospitalization), 6 months and 12 months postinfection (CCER 2020-00835). Control children with uncomplicated COVID-19 were drawn from the "understanding COVID" study (CCER 2020-00516)[3] for the baseline (T0), T6 and T12 examinations and from the SEROCOV-KIDS (CCER 2021-01973) for the T12 examination.[4] Importantly, both the MIS-C children and the controls had been infected during the same time-period, when the original strain and the antigenically similar alpha variant of SARS-CoV-2 circulated in Switzerland. Children who had been vaccinated during the study were excluded from the analysis. Methodological details were previously described.[2]

IgA antibodies levels underwent a rapid decrease at 6 months postinfection and remained stable at 12 months. There was no apparent difference in IgA antibodies levels and trajectories between the MIS-C children and children with uncomplicated COVID-19. At 6 months, MIS-C children reached neutralization titers like those of children with uncomplicated COVID-19 and the levels remained stable by 12 months postinfection. IgG antibody levels decreased slowly for most of the SARS-CoV-2 antigens at 6 months and 12 months in both groups. The level of S2-specific antibodies, however, remained higher than those of other IgGs (see Fig. 1).

Overall, IgG, IgA and neutralizing antibodies against SARS-CoV-2 remain high up to 1-year postinfection, irrespective of whether children had developed MIS-C. The fact that the initially strongest IgA and neutralizing antibody response was lost at 6 months postinfection, suggests that those previous observations probably reflect the consequences of the gastrointestinal inflammation, which is a prominent feature of MIS-C children.[5]

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