University of Nebraska Medical Center
Nebraska Medicine

Graduate Medical Education Research Journal

Volume 5
Issue 2 *Incremental*

Article 5

October 2023

Rare Streptococcus intermedius Central Nervous System Septic Emboli: A Case Report and Review of Literature

Jonathan Herskovitz
University of Nebraska Medical Center

Cristina J. Torres
University of Nebraska Medical Center

Bryan Walker
University of Nebraska Medical Center

Jasmine R. Marcelin
University of Nebraska Medical Center

Rare Streptococcus intermedius Central Nervous System Septic Emboli: A Case Report and Review of Literature

Abstract

We report a case of a male in his thirties who presented with rapidly progressive encephalopathy, mediastinal abscess, and multiple ring-enhancing lesions throughout the brain. Extensive evaluation revealed *Streptococcus intermedius* septic emboli to the brain from dental sources via a right-to-left anatomic shunt. The patient completed an 11-week course of IV antibiotic therapy after which he made a near complete recovery. We provide a comprehensive review of the literature with *Streptococcus intermedius* CNS septic emboli and source of infection.

Keywords

CNS septic emboli, S. intermedius, odontogenic

Rare Streptococcus Intermedius Central Nervous System Septic Emboli: A Case Report and Review of Literature

Jonathan Herskovitz[1], Cristina J. Torres[1], Bryan Walker[1], Jasmine R. Marcelin[1]
[1]College of Medicine, University of Nebraska Medical Center, Omaha, NE, USA

https://doi.org/10.32873/unmc.dc.gmerj.5.2.003

Abstract

We report a case of a male in his thirties who presented with rapidly progressive encephalopathy, mediastinal abscess, and multiple ring-enhancing lesions throughout the brain. Extensive evaluation revealed *Streptococcus intermedius* septic emboli to the brain from dental sources via a right-to-left anatomic shunt. The patient completed an 11-week course of IV antibiotic therapy after which he made a near complete recovery. We provide a comprehensive review of the literature with *Streptococcus intermedius* CNS septic emboli and source of infection.

Keywords

CNS septic emboli, *S. intermedius*, odontogenic

Background

Streptococcus intermedius is a Gram-positive coccus in the *Streptococcus milleri (anginosus)* group that also includes *S. anginosus* and *S. constellatus*. The *milleri* subgroup of Viridans group Streptococcus colonize the oropharynx and gut, but often cause invasive diseases of the head and neck, thorax, abdomen, and central nervous system via local translocation and hematogenous dissemination. Right-to-left anatomic shunts in the heart or lungs also predispose patients to paradoxical septic emboli to the brain.

Case

A man in his thirties presented febrile (38.3°C) and rapidly progressive encephalopathy following one-week of fevers, malaise, nausea, and vomiting. He had a two-day period where he appeared to improve but then two days prior to admission he developed significant headache, vomiting and an inability to sit upright, subsequently becoming confused, incontinent of urine, and then obtunded within the 24 hours prior to presentation. Pertinent past medical history included dental caries and alcohol use disorder. Prior to the onset of this presentation, he had no other neurologic symptoms reported by family. On physical exam he was obtunded but arousable, and unable to follow commands. He had bilateral horizontal nystagmus with rightward gaze, inability to track past midline, and left hemiparesis, without nuchal rigidity. Initial workup revealed leukocytosis (WBC 26,000 cells/μL) with elevated cerebrospinal fluid (CSF) neutrophil-predominant (80%) white blood cell count (5910 cells/μL), elevated protein (173 mg/dL), and normal glucose (65 mg/dL). Computed Tomography (CT) chest/abdomen/pelvis showed a 3.7 cm mid-esophageal mass with multiple foci of eccentric gas. Brain MRI showed innumerable ring-enhancing lesions, consistent with septic emboli (**Figure 1**). Neurology was consulted and determined that his neurologic findings on exam were likely due to the innumerable septic emboli including frontal lobe lesions with considerable surrounding edema. He underwent electroencephalogram (EEG) testing and was not diagnosed with active seizure activity, however prophylactic antiepileptic treatment started in the ED was continued given the extent of cerebral edema. The patient was intubated, blood cultures obtained, and started empirically on standard central nervous system (CNS) doses of IV acyclovir, vancomycin, ceftriaxone, metronidazole, and dexamethasone.

CSF meningitis and sputum respiratory pathogen PCR panels, bacterial and fungal cultures of blood and CSF, and serologies for HIV, *Histoplasma*, *Cryptococcus*, *Coccidioides*, and *Blastomycosis* were negative. Transthoracic and transesophageal echocardiograms revealed a patent foramen ovale (PFO) without valvular vegetations. Positron emission tomography (PET)/CT imaged a gas-containing mediastinal abscess in the right border of the esophagus and mainstem bronchus and extensive brain septic

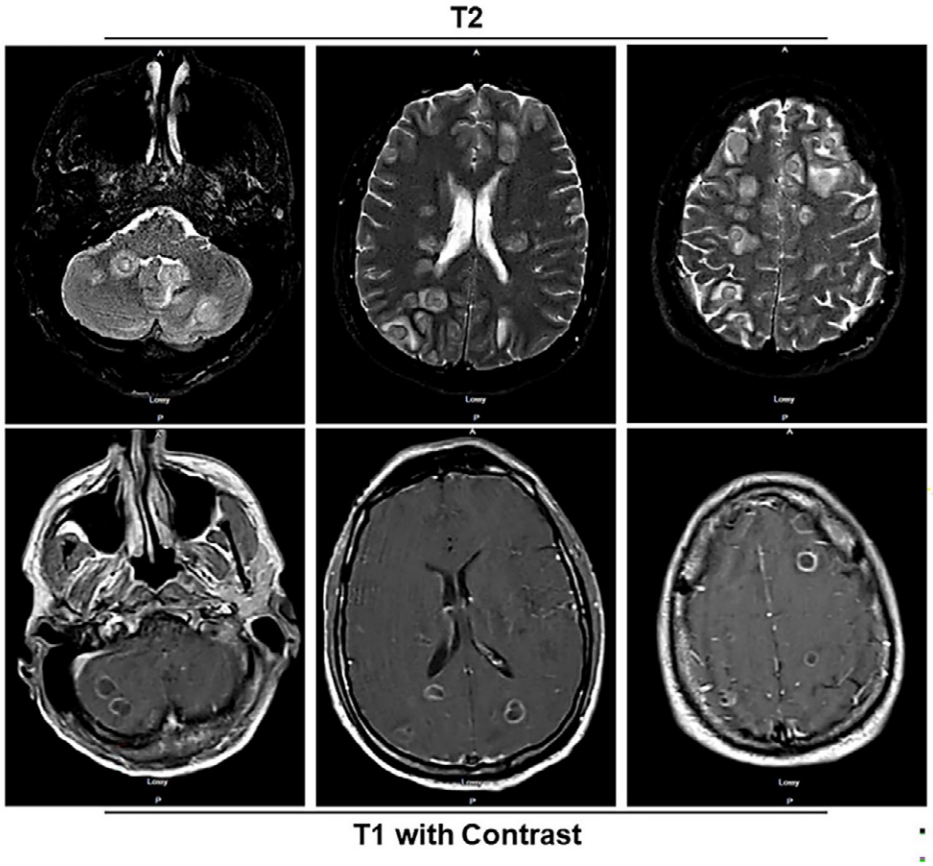

Figure 1. MRI of a 34-year-old patient with diffuse ring-enhancing lesions of the brain. T2 weighted (top) and T1 with contrast (bottom) MRI images of septic emboli to the brain.

emboli without evidence of malignancy as a potential cause of the CNS ring-enhancing lesions. Mediastinal abscess culture via endoscopic ultrasound-guided (EUS) biopsy yielded *Streptococcus intermedius*, *Streptococcus mitis oralis* and eventual *Rothia mucilaginosa* and *Alloscordovia amniocolens* on hospital day four. Cytology of fine needle aspirate from a lymph node adjacent to the mediastinal abscess showed filamentous bacteria consistent with *Actinomyces* or *Nocardia* species.

Dental evaluation post-extubation on hospital day 5 revealed six non-salvageable carious teeth. Further collateral history informed that the patient suffered from poor dental care prior to hospitalization due to lack of insurance and frequently consumed alcohol to the point of blacking out and vomiting. These historical and physical findings point towards mediastinal abscess formation following an aspiration event. Broad spectrum antimicrobials (vancomycin, ceftriaxone, metronidazole, and acyclovir) were progressively narrowed over 6 days to ceftriaxone, at which point the patient was extubated and vocally responsive. Despite his clinical improvement, leukocyte counts remained elevated. Repeat MRI demonstrated increases in the size of brain abscesses and detected a new T9-T10 intramedullary spinal cord abscess. Neurosurgical biopsy of the spinal cord abscess was deferred due to lack of radiographic evidence of epidural phlegmon or cord compression. Antibiotic coverage was expanded to trimethoprim-sulfamethoxazole and imipenem to cover for possible CNS *Nocardia* infection after filamentous bacteria had been seen on mediastinal abscess cytology. He underwent tooth extraction on hospital day nine and video-assisted thoracoscopic surgery (VATS) drainage of the mediastinal abscess on hospital day 10. The following day, patient plasma collected for Karius® metagenomic next-generation sequencing, (which can detect over 1000 pathogens using microbial cell-free DNA), resulted positively for *Streptococcus intermedius*.

Antibiotics were narrowed to ceftriaxone due to its excellent tissue permeability and simplified dosing schedule compared to penicillin G and ampicillin-sulbactam yet equivalent efficacy against Viridans group *Streptococci*.[1,2] The patient was discharged after 49 days of inpatient management on a 4-week regimen of IV cefepime and oral metronidazole. Cefepime was chosen as the final beta-lactam because of persistent transaminitis that resolved with ceftriaxone discontinuation. Final inclusion of metronidazole accorded with recommendations for *Streptococcus milleri* group abscesses.[1] Repeat MRI at 10 weeks after initial presentation demonstrated a reduction in the size of brain emboli.

Improvement on cephalosporins rather than trimethoprim-sulfamethoxazole further supported CNS infection by *Streptococcus intermedius* rather than often cephalosporin-resistant *Nocardia*. *Actinomyces* brain-coinfection could not be definitively excluded, however would portend a higher morbidity and mortality not observed in the care of this patient. Following three weeks of acute rehabilitation, the patient now communicates freely and ambulates independently with a cane. His PFO remains open due to low present risk for septic emboli and DVT/PE recurrence.

Literature Review Methods

A MEDLINE literature search performed between March and July 2022 for terms "*S. intermedius*," "*Strep intermedius*," "*Streptococcus intermedius*," "brain," and "CNS" revealed 146 primary article results published between 1999 and 2022. Of these, 41 patients were described in 36 case reports and case series in the English language were reviewed. To evaluate similar treatment parameters and patient outcomes to that of our patient, cases lacking brain-involvement (n=1), author indication of confirmed polymicrobial CNS infection (n=3), or infective endocarditis (n=2) for which management differs from that of CNS infection,[1] were excluded from further review.

Discussion

Brain abscess has an annual incidence of 1 in 100,000 persons, with *Streptococcus milleri* group as a common bacterial cause.[3] In adults, the median age of CNS septic emboli due to *Streptococcus intermedius* was 47 years old (range 20-72 years). Our review indicates a 61% male predominance with a 96% survival rate after surgical debridement and appropriate antibiotics. Bacterial culture of CNS samples remained more common than molecular-based methods of *Streptococcus intermedius* identification (29 of 41 reported patients). However, only six patients were found to be blood-culture positive.[4-8] A summary of available case reports is available in **Table 1**.[4-39] We suspect scarcity of *Streptococcus intermedius* blood culture growth in these cases relates to urgent initiation of antibiotics prior to blood culture, or as with our patient, the strain's propensity for focal abscess formation.[40] Cephalosporins and monobactams were the most heavily utilized among published reports. Given *Streptococcus milleri* group's 98% sensitivity to beta-lactams and frequent co-infection with anaerobes, expert recommendations[1] favor ceftriaxone (2 g q12h) plus intravenous metronidazole (500 mg q8h) over penicillin G plus intravenous metronidazole or ampicillin-sulbactam due to reduced frequency of dosing. Median duration of antibiotic therapy was 7.5 weeks (range 2-32 weeks), though experts advise continuation of intravenous antibiotics until radiographic and clinical improvement are achieved.[1] Most patients saw partial or complete recovery of function following pharmacotherapy.

To our knowledge, this marks the fifth report of paradoxical *Streptococcus intermedius* emboli that mobilized from dental sources to the brain via a PFO.[23,34,36] Other cardiac malformations and pulmonary AV fistulae represent alternate modes of *Streptococcus intermedius* embolization to the CNS. In our literature review, 16/41 (39%) cases had multiple CNS abscesses. We hypothesize that passage of septic thrombophlebitis through a PFO leads to showering of the brain with bacteria under high arterial pressure. Our case is unique in that the patient had both a PFO and a large mediastinal abscess. While we hypothesize that the brain embolization involved passage of bacteria through his PFO, it is impossible to tell whether this was primarily from his dental caries or secondarily from the mediastinal abscess. However, given the collateral history and overall presentation, we suspect that the likely sequence of events included dental caries leading to mediastinal abscess after aspiration event, which then led to transient bacteremia, passage through PFO, and subsequent brain emboli. Disseminated paradoxical septic emboli of the brain have been described in PFO-proven cases of *Streptoccocus intermedius*[23,36] and Lemierre's syndrome.[41]

In summary, *Streptococcus intermedius* establishes distal abscesses of the brain often via direct spread from odontogenic infections and less commonly through right-to-left anatomic shunts. Concomitant bacteremia appears to be uncommon in this syndrome, therefore negative blood cultures should not eliminate the possibility of infectious etiologies for ring-enhancing lesions. Prompt multidisciplinary medical care with appropriate antimicrobials and source control facilitated a favorable prognosis for our patient and the majority of patients included in our literature review. ■

Table 1. Literature review of case reports of *Streptococcus intermedius* septic emboli to the brain

Lead Author (year)	Age (yrs.) / Sex	CNS Imaging	Oral Source	Cardiac Defect	S. intermedius. Blood Culture (+)	CNS ID Method	Regimen* (initial [intermediate] / final)	Abx Duration (wks)	Outcome
Herskovitz (2022) [this case report]	34 / M	Diffuse ring-enhancing lesions, T9-T10 spinal cord abscess	Yes	Yes (PFO)	No	Cell-free DNA next-generation sequencing	CRO, VAN, MTZ, ACV [TMP-SMX, IPM] / FEP, MTZ	11	Survived (complete recovery)
Gupta (2022)[9]	43 / F	1 ring-enhancing lesion (temporal lobe), edema	No (IUD associated)	NR	NR	culture	CRO, VAN, MTZ / CRO	7	Survived
Hauser (2022)[10]	26 / M	14 supratentorial and right cerebellar ring-enhancing lesions	No	No	No	16S rRNA	CRO, VAN, MTZ / CRO	32	Survived (complete recovery)
Hirose (2022)[11]	36 / M	T12-L12 ring-enhancing intramedullary lesion	No	Yes (right superior vena cava — left atrial shunt)	No	CSF culture	MEM, VAN / AMP	6	Survived (complete recovery)
Oleinikov (2022)[12]	11 / F	Posterior fossa empyema with hydrocephalus	Yes	NR	No	culture	MEM, VAN [MEM, LZD] / LZD	12	Survived
Tkacz (2022)[6]	6 / M	Thickened mucosa of sphenoid sinus; no brain abscess	No	NR	Yes	CSF culture	CRO, VAN / CRO	2	Survived (complete recovery)
Verma (2021)[13]	68 / M	1 ring-enhancing lesion (medulla), edema	Yes	No	No	culture	NR / CRO, MTZ	18	Survived (complete recovery)
Fransson (2021)[14]	34 / M	multiple ring-enhancing lesions, ventriculitis, edema	Yes	No	No	16S rRNA	MEM, VAN, ACV [MEM, VAN, MTZ +/- TMP-SMX +/- RIF] / MEM, VAN, MTZ	6	Survived (partial recovery)
Mintz (2021)[15]	12 / F	1 ring-enhancing lesion (frontal parasagittal)	NR	NR	NR	culture	CRO, MTZ	4	Survived (complete recovery)
Shibata (2021)[16]	62 / M	1 ring-enhancing lesion (frontal lobe)	Yes (periodontitis)	No	No	culture	MEM, VAN / CRO	NR	Deceased (due to cancer comorbidity)
	68 / M	2 ring-enhancing lesions, edema	Yes	No	No	culture	MEM	NR	Deceased (due to cancer comorbidity)
Yuen (2021)[17]	65 / F	1 ring-enhancing brain lesion (frontal lobe)	Yes	NR	NR	culture	NR	6	Survived (partial recovery)
Gao (2020)[18]	55 / M	1 ring-enhancing lesion (peri-ventricular) + edema	No	No (Pulmonary AV fistula)	No	CSF metagenomic next-generation sequencing	CRO, VAN [MTZ] / PEN G	9	Survived (complete recovery)
Kudo-Kubo (2020)[19]	1.25 / F	3 ring-enhancing lesions (parietal, occipital lobes)	No	Yes (transposition of great vessels, VSD)	No	culture	MEM, VAN / PEN G	16	Survived
Diaz (2019)[20]	27 / M	1 peripherally enhancing lesion (left front lobe mass), edema, uncal herniation	Probable	No (Pulmonary AV malformations)	No	culture	CRO	8	Survived
Issa (2019)[21]	12 / NR	left holoencephalic hypodensity (CT)	No (sinusitis)	NR	NR	culture + whole-genome sequencing of isolate	CRO	NR	Survived (complete recovery)
Al Moussawi (2018)[22]	56 / F	1 ring-enhancing lesion + edema	Yes (recent tooth extraction)	NR	NR	culture	CRO, VAN, MTZ	NR	Survived (complete recovery)
Viviano (2018)[23]	28 / M	2 ring-enhancing brain lesions (occipital and parietal lobes)	Yes	Yes (PFO)	No	culture	CRO, VAN, MTZ / CLI, AMC	15	Survived
Khaja (2017)[24]	72 / F	ring-enhancing lesion (left temporal lobe) + edema	No	NR	NR	culture	CRO, AMP, VAN / SAM	5	Survived (complete recovery)
Nayfe (2017)[25]	53 / F	1 ring-enhancing lesion (right thalamus), edema, herniation	NR	NR	NR	culture	NR	NR	NR
Tsuang (2017)[26]	68 / F	1 ring-enhanced cystic lesion (thalamus), edema	NR	NR	No	16s rRNA	CRO, MTZ / CRO	8	Survived (complete recovery)

Lead Author (year)	Age (yrs.) / Sex	CNS Imaging	Oral Source	Cardiac Defect	S. intermedius. Blood Culture (+)	CNS ID Method	Regimen* (initial [intermediate] / final)	Abx Duration (wks)	Outcome
Basyuni (2015)[27]	53 / M	1 peripherally enhancing lesion (right internal capsule, thalamus, midbrain), edema, mass effect	Yes	NR	No	culture	CRO, MTZ / MEM	NR	Deceased
Yakut (2015)[28]	10 / M	right-sided mastoiditis and right cerebellar abscess	No (mastoiditis)	No	No	Cerebellar drainage and VITEK mass spectrometry	TZP, VAN / MEM, VAN	6	Survived (complete recovery)
Trabue (2013)[29]	36 / M	2 ring-enhancing lesions (parieto-occipital cortex)	Yes	NR	NR	culture	NR	NR	NR
Hanna (2013)[4]	46 / M	2 ring-enhancing lesions (fronto-parietal, parietal), edema	No	No	Yes	culture	NR / CRO, MRO	6	Survived (partial recovery)
Saito (2012)[30]	70 / F	Diffuse ring-enhancing brain lesions	NR	NR	No	16S rRNA	MEM, VAN [CRO, Amp] / LVX	12	Survived (complete recovery)
Esposito (2011)[31]	3 / F	1 hypodense lesion (parietal lobe) + edema	No	NR	No	culture	CRO /CRO, MTZ	NR	Survived
Lee (2011)[5]	47 / F	1 ring-enhancing lesion (left frontal lobe)	NR	Yes (left superior vena cava - left atrial shunt)	Yes	culture	PEN G, MTZ / ETP	8	Survived (complete recovery)
Malyiyil (2011)[32]	21 / M	3 ring-enhancing lesions (frontal, occipital lobes)	No	No	Yes	culture	CRO, VAN / ETP	12	Survived (complete recovery)
Herskovitz (2009)[33]	22 / M	13 ring-enhancing lesions	Yes (tongue piercing)	NR	No	culture	PEN / PEN, CHL	5	Deceased
Jan (2009)[34]	47 / M	15-20 diffuse ring-enhancing lesions	Yes	Yes (PFO)	No	culture	NR	NR	Survived (complete recovery)
Syros (2009)[35]	20 / M	1 ring-enhancing brain lesion (left parietal lobe)	No	Yes (PFO)	No	culture	CRO, MTZ	6	Survived (complete recovery)
Petti (2008)[36]	6 / M	diffuse ring-enhancing lesions	Yes (dental caries)	Yes (Ebstein anomaly, PFO)	No	16S rRNA	CRO, VAN / MEM	13	Survived (partial recovery)
	16 / M	diffuse ring-enhancing lesions	No	No	No	No (tracheal 16S rRNA)	CRO, VAN, ACV [CRO, VAN, MTZ] / CRO, RIF	16	Survived (partial recovery)
	21 / M	diffuse ring-enhancing lesions, hydrocephalus	No (sinusitis)	NR	No	16S rRNA	CRO, VAN, MTZ [+ AMB] / Gram (+) directed therapy	6	Survived (complete recovery)
Tran (2008)[7]	16 / F	1 ring-enhancing brain lesion (frontal lobe)	No (sinusitis)	NR	Yes	culture & 16S rRNA	CRO, MTZ / CRO	8	Survived
Pompucci (2007)[37]	65 / F	brain and spinal subdural empyema	NR	NR	No	empyema culture	RIF, VAN / AMP	8	Survived (complete recovery)
Wagner (2006)[8]	39 / ?	2 abscesses (frontal, temporal lobes and pons)	Yes (periodontitis)	No	Yes	culture	CRO, MTZ / PEN G, MTZ	NR	Survived (complete recovery)
Khatib (2000)[38]	55 / M	bilateral ring-enhancing lesions	No (lobar pneumonia)	NR	No	Autopsy	CRO, AMP	NR	Deceased
Yamamoto (1999)[39]	12 / M	1 frontal lobe mass extending to ethmoid and frontal sinuses	No (sinusitis)	NR	No	culture	aspoxicillin, MOX / PIP, CMZ	4	Survived (complete recovery)
	52 / M	1 ring-enhancing brain lesion (frontal lobe) + edema	NR	NR	No	culture	cefotiam / panipenem	5	Survived (complete recovery)

Author Contributions

JH composed initial manuscript draft and figures. CT, BW, and JRM revised manuscript all drafts. JRM submitted final manuscript for publication.

Potential conflicts of interest

JRM is a volunteer member of the IDSA Board of Directors. JRM received consultative honorarium in 2021 for serving on a Pfizer Global Medical Grants/ Mayo Clinic Global Bridges Antimicrobial Stewardship Grant review panel and from Pew Charitable trust in 2022, not related to this project. All other authors: No reported conflicts.

Funding Source

No funding was used for this case report.

Financial Disclosure

None reported.

References

1 Stout J, D K. Infections due to the Streptococcus anginosus (Streptococcus milleri) group. *Wolters Kluwer*; 2022.

2 Wo S, Dubrovskaya Y, Siegfried J, Papadopoulos J, Jen SP. Clinical Outcomes of Ceftriaxone vs Penicillin G for Complicated Viridans Group Streptococci Bacteremia. *Open Forum Infect Dis.* 2021;8(1):ofaa542.

3 Mishra AK, Fournier PE. The role of Streptococcus intermedius in brain abscess. *Eur J Clin Microbiol Infect Dis.* 2013;32(4):477-83.

4 Hanna MS, Das D. Oesophageal adenocarcinoma presenting with multiple Streptococcus intermedius cerebral abscesses. *J Gastrointest Cancer.* 2014;45 Suppl 1:18-21.

5 Lee MS, Pande RL, Rao B, Landzberg MJ, Kwong RY. Cerebral abscess due to persistent left superior vena cava draining into the left atrium. *Circulation.* 2011;124(21):2362-4.

6 Tkacz K, Piwowarczyk A, Podsiadly E, Kuchar E. Streptococcus intermedius Acute Meningitis in an Immunocompetent Child. *Pediatr Infect Dis J.* 2022.

7 Tran MP, Caldwell-McMillan M, Khalife W, Young VB. Streptococcus intermedius causing infective endocarditis and abscesses: a report of three cases and review of the literature. *BMC Infect Dis.* 2008;8:154.

8 Wagner KW, Schön R, Schumacher M, Schmelzeisen R, Schulze D. Case report: brain and liver abscesses caused by oral infection with Streptococcus intermedius. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006;102(4):e21-3.

9 Gupta S, Kasule SN, Seville MT. Cerebral abscess with Streptococcus intermedius as a complication of pelvic inflammatory disease in the setting of intrauterine device use. *IDCases.* 2022;27:e01454.

10 Hauser N, Werzen A, Rapaka RR. The Brief Case: Streptococcus intermedius Brain Abscesses in an Otherwise Healthy Young Man Diagnosed by 16S rRNA Gene Sequencing. *J Clin Microbiol.* 2022;60(1):e0197020.

11 Hirose S, Sudo N, Okada M, Natori N, Akimoto T, Hara M, et al. Intramedullary spinal cord abscess associated with right-to-left shunt via right superior vena cava draining into left atrium: A case report. *Medicine* (Baltimore). 2022;101(26):e29740.

12 Oleinikov B, Musa G, Livshitz MI, Kolcheva M, Ramirez MJE, Nurmukhametov R, et al. Surgical Management of a Pediatric Infratentorial Subdural Empyema as a Complication of Parapharyngeal Abscess. *Cureus.* 2022;14(5):e25270.

13 Verma A, Qutab S, Baig M. Medullary brain abscess secondary to dental procedure caused by Streptococcus intermedius. *BMJ Case Rep.* 2021;14(6).

14 Fransson M, Hellden A, Ostholm Balkhed A, Nezirevic Dernroth D, Ha M, Haglund M, et al. Case Report: Subtherapeutic Vancomycin and Meropenem Concentrations due to Augmented Renal Clearance in a Patient With Intracranial Infection Caused by Streptococcus intermedius. *Front Pharmacol.* 2021;12:728075.

15 Mintz JL, Jameson MB, Akinseye L, Los EA. Pediatric diabetic ketoacidosis presenting with Streptococcus intermedius brain abscess. *J Pediatr Endocrinol Metab.* 2021;34(6):817-20.

16 Shibata T, Hashimoto N, Okura A, Mase M. Brain abscess of odontogenic origin in patients with malignant tumors: A report of two cases. *Surg Neurol Int.* 2021;12:417.

17 Yuen J, Muquit S. A woman with headache, hemiplegia, and recent toothache. *BMJ.* 2021;372:n10.

18 Gao LY, Xu GR, Dai TJ. Precision diagnosis and therapy of a case of brain abscesses associated with asymptomatic pulmonary arteriovenous fistulas. *BMC Infect Dis.* 2020;20(1):370.

19 Kudo-Kubo A, Shimakawa S, Odanaka Y, Ikeda N, Kitahara H, Toshikawa H, et al. Multiple brain abscesses with good prognosis in an infant with cyanotic congenital heart disease: a case report. *J Med Case Rep.* 2020;14(1):111.

20 Diaz J, Rose A, Meader S. Acute Encephalopathy Leading to a New Diagnosis of Hereditary Hemorrhagic Telangiectasia in a Young Male. Am J Med. 2020;133(6):e233-e6.

21 Issa E, Salloum T, Panossian B, Ayoub D, Abboud E, Tokajian S. Genome Mining and Comparative Analysis of Streptococcus intermedius Causing Brain Abscess in a Child. *Pathogens.* 2019;8(1).

22 Al Moussawi H, Krzyzak M, Awada Z, Chalhoub JM. Streptococcus Intermedius Brain and Diverticular Abscesses After Dental Manipulation: A Case Report. *Cureus.* 2018;10(1):e2061.

23 Viviano M, Cocca S. Multiple brain abscesses after professional tooth cleaning: Case report and literature review. *J Stomatol Oral Maxillofac Surg.* 2018;119(5):432-5.

24 Khaja M, Adler D, Lominadze G. Expressive aphasia caused by Streptococcus intermedius brain abscess in an immunocompetent patient. *Int Med Case Rep J.* 2017;10:25-30.

25 Nayfe R, Ascha MS, Rehmus EH. Esophageal Squamous Cell Carcinoma Presenting with Streptococcus intermedius Cerebral Abscess. Case Rep *Pathol.* 2017;2017:5819676.

26 Tsuang FY, Lin YT, Yen DH, Teng LJ, Tsai JC. Rapid identification of Streptococcus intermedius by multiplex polymerase chain reaction 1 week before culture positivity in a patient with antibiotic-treated thalamic brain abscess. *J Microbiol Immunol Infect.* 2017;50(4):549-51.

27 Basyuni S, Sharma V, Santhanam V, Ferro A. Fatal thalamic abscess secondary to dental infection. *BMJ Case Rep.* 2015;2015.

28 Yakut N, Kadayifci EK, Karaaslan A, Atici S, Akkoc G, Ocal Demir S, et al. Brain abscess due to Streptococcus intermedius secondary to mastoiditis in a child. *Springerplus*. 2015;4:809.

29 Trabue C, Pearman R, Doering T. Pyogenic brain and lung abscesses due to Streptococcus intermedius. *J Gen Intern Med.* 2014;29(2):407.

30 Saito N, Hida A, Koide Y, Ooka T, Ichikawa Y, Shimizu J, et al. Culture-negative brain abscess with Streptococcus intermedius infection with diagnosis established by direct nucleotide sequence analysis of the 16s ribosomal RNA gene. *Intern Med.* 2012;51(2):211-6.

31 Esposito S, Bosis S, Dusi E, Cinnante C, Principi N. Brain abscess due to Streptococcus intermedius in a 3-year-old child. *Pediatr Int.* 2011;53(6):1104-5.

32 Maliyil J, Caire W, Nair R, Bridges D. Splenic abscess and multiple brain abscesses caused by Streptococcus intermedius in a young healthy man. *Proc* (Bayl Univ Med Cent). 2011;24(3):195-9.

33 Herskovitz MY, Goldsher D, Finkelstein R, Bar-Lavi Y, Constantinescu M, Telman G. Multiple brain abscesses associated with tongue piercing. *Arch Neurol.* 2009;66(10):1292.

34 Jan F, Hafiz AM, Gupta S, Meidl J, Allaqaband S. Brain abscesses in a patient with a patent foramen ovale: a case report. J Med Case Rep. 2009;3:9299.

35 Syros G, Briasoulis A, Psevdos G. Suspicious seizures: Uncommon complication of PFO/ASA. *J Cardiol Cases.* 2011;3(3):e170-e2.

36 Petti CA, Simmon KE, Bender J, Blaschke A, Webster KA, Conneely MF, et al. Culture-Negative intracerebral abscesses in children and adolescents from Streptococcus anginosus group infection: a case series. *Clin Infect Dis.* 2008;46(10):1578-80.

37 Pompucci A, De Bonis P, Sabatino G, Federico G, Moschini M, Anile C, et al. Cranio-spinal subdural empyema due to S. intermedius: a case report. *J Neuroimaging.* 2007;17(4):358-60.

38 Khatib R, Ramanathan J, Baran J, Jr. Streptococcus intermedius: A cause of lobar pneumonia with meningitis and brain abscesses. *Clin Infect Dis.* 2000;30(2):396-7.

39 Yamamoto M, Fukushima T, Ohshiro S, Go Y, Tsugu H, Kono K, et al. Brain abscess caused by Streptococcus intermedius: two case reports. *Surg Neurol.* 1999;51(2):219-22.

40 Claridge JE, 3rd, Attorri S, Musher DM, Hebert J, Dunbar S. Streptococcus intermedius, Streptococcus constellatus, and Streptococcus anginosus ("Streptococcus milleri group") are of different clinical importance and are not equally associated with abscess. *Clin Infect Dis.* 2001;32(10):1511-5.

41 Vendeville A, Winzer K, Heurlier K, Tang CM, Hardie KR. Making 'sense' of metabolism: autoinducer-2, LuxS and pathogenic bacteria. *Nat Rev Microbiol.* 2005;3(5):383-96.