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Case Series

Campylobacter spp. in Brain Abscesses: Four Cases and a Review of Previous Literature

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Abstract

Introduction: Four cases of brain abscesses with *Campylobacter rectus* and *C. gracilis* were registered at Copenhagen University Hospital within a short period. Brain abscesses are serious, often life-threatening, conditions. *C. rectus* and *C. gracilis* are oral *Campylobacters* which may cause periodontitis, oral abscesses and sinusitis; a frequent focus for brain abscesses.

Aim of the Study: The aim of this study was to search the Microbiology database and review the literature on *Campylobacter* spp. and brain abscesses to clarify this rare condition.

Materials and Methods: The Microbiology database was searched for *Campylobacter* spp. and abscesses. Three databases were searched for *Campylobacter* spp. and brain abscesses.

Results. In the Microbiology database four cases with *Campylobacter* spp. in brain abscesses were found: A 42-year-old male with periodontist had a brain abscess with *C. gracilis* and *Fusobacterium* spp. A 71-year-old woman had a brain abscess with *C. rectus* and *F. nucleatum* believed to arise from a middle ear infection. A 72-year-old man with a dental abscess had a brain abscess with *C. rectus*, *Streptococcus anginosus* and *F. nucleatum* and a 62-year-old woman with a tooth abscess had a brain abscess with *C. rectus*, *Staphylococcus epidermidis* and *S. anginosus*. The literature review revealed two patients with brain abscesses with *C. rectus*, one with brain abscess with *C. gracilis,* and one brain abscess with *C. concisus*.

Conclusion: Even though it is a rare condition to find *Campylobacter* spp. in brain abscesses it may be of interest to look for *Campylobacter* spp. as they are difficult to culture and may sometimes be overlooked.

Keywords: *Campylobacter spp; Brain Abscesses*

Introduction

Campylobacter rectus and *Campylobacter gracilis* are hydrogen dependent, Gram-negative rods, that show optimal growth under anaerobic conditions. *C. rectus* and *C. gracilis* are straight rods which differentiate them from most other *Campylobacter* spp. that are curved or spiral shaped rods [1]. They both occur naturally in the human oral flora, especially in high quantities in cases of periodontitis, but they have also been isolated from extra oral sites [1]. *C. gracilis* has been found especially in deep-seated abscesses close to the head and neck, whereas *C. rectus* has been isolated from sites like plaque from atherosclerosis [1,2].

In the past ten years (2011 - 2021), there has been registered four brain abscesses with *Campylobacter* spp. detected in them at Copenhagen University Hospital. *C. rectus* was detected in three of the brain abscesses and *C. gracilis* in one.

A brain abscess is an infection in the brain parenchyma [3]. This type of infection begin as cerebritis and later becomes more localized with development of necrosis and a capsule around it. Other infections like otitis media, sinusitis and tooth abscesses are often predisposing to the development of a brain abscess. It is proposed that these infections spread to the brain via the blood [3]. Brain abscesses are rare with a general incidence of 1,3 pr. 100.000 people per a year. Though, this type of infection is rare, it is life threatening and can cause symptoms like aphasia, loss of muscle control and local paralysis [3]

Case Reports

Patient case 1

A previously healthy 42-year-old man was hospitalized following a generalized seizure with a slight fever. Computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated two adjacent round contrast-enhancing tumors in the left frontal lobe with severe perifocal edema. After treatment with anti-epileptic drugs, the patient was asymptomatic. A sub-acutely performed CT-guided stereotactic puncture extricated a few milliliters of pus. Cultures of the pus did not show bacterial growth, however subsequent 16S rRNA PCR amplification test revealed *Campylobacter gracilis* and *Fusobacterium* species. Initial antibiotic treatment was intravenous meropenem, fucidic acid and metronidazole. A thorough search for a bacterial infection site was performed without certain finding of an extracranial infection focus. A thoracic CT demonstrated a minor infiltration in the lung, which diminished with the antibiotic treatment. Dental examination revealed chronic periodontitis. The patient received a total of 7 weeks of antibiotics and continued to be asymptomatic. He was able to begin work, when his antibiotic treatment was finished.

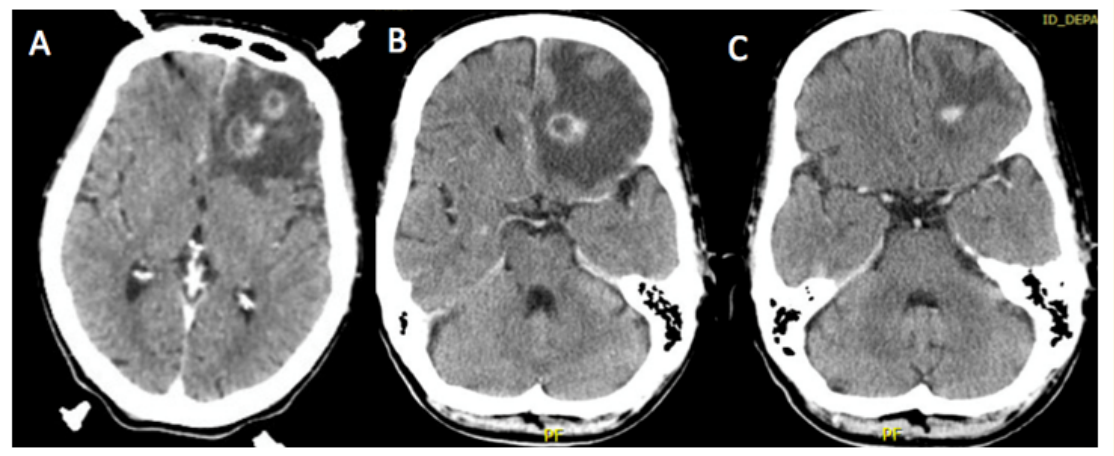

Figure 1: *A: Per-operative CT with contrast showing two enhancing abscesses in the left frontal lobe with surrounding edema. B: Contrast enhanced CT 5 days following surgery with no change in edema and abscess configuration. C: CT 7 weeks following operation with only minimal edema and minor focal contrast enhancement.*

Patient case 2

A 71-year-old woman, previously treated with lumpectomy for a breast adenocarcinoma, presented with several months of vomiting, intensifying headaches, left sided otalgia, and was admitted due to weight loss of 11 kilogram within a few months and excessive nausea. Upon admission the examination did not reveal any neurological deficit. CT of the cerebrum showed a tumor with perifocal edema of the left cerebellopontine angle. The patient deteriorated rapidly in consciousness after admission. An acute MRI with contrast demonstrated a multilobulated abscess in the left cerebellopontine angle originating from the left acoustic meatus and pars petrosa with compression of the brainstem, cerebellum and fourth ventricle, the latter causing supratentorial hydrocephalus. Acute surgical decompression with partial surgical drainage of the abscess and insertion of an external ventricular catheter to relieve the hydrocephalus was performed. Following surgery, the patient required continuous sedation and mechanical ventilation in a respirator. Post-operative CT revealed severe edema with critical compression of the brain stem and surgical decompressive craniectomy of the posterior fossa compartment was performed 5 days following the primary surgery. Cultures from the drained abscess revealed moderate growth of *Campylobacter rectus* and *Fusobacterium nucleatum* believed to arise from a middle ear infection. The patient was treated with intravenous meropenem and metronidazole with a good response on biochemical parameters such as CRP and leukocytes. Due to the patient's brain stem compression the patient had severe neurological deficits and required a tracheostomy and slow weaning from the respirator. MRI demonstrated regression of the abscess but also infarction and minor hemorrhage in the left side of the brainstem. The patient received a total of 9 weeks of antibiotics. At follow up, one year from admission, the patient was bedridden and had severe neurological deficits.

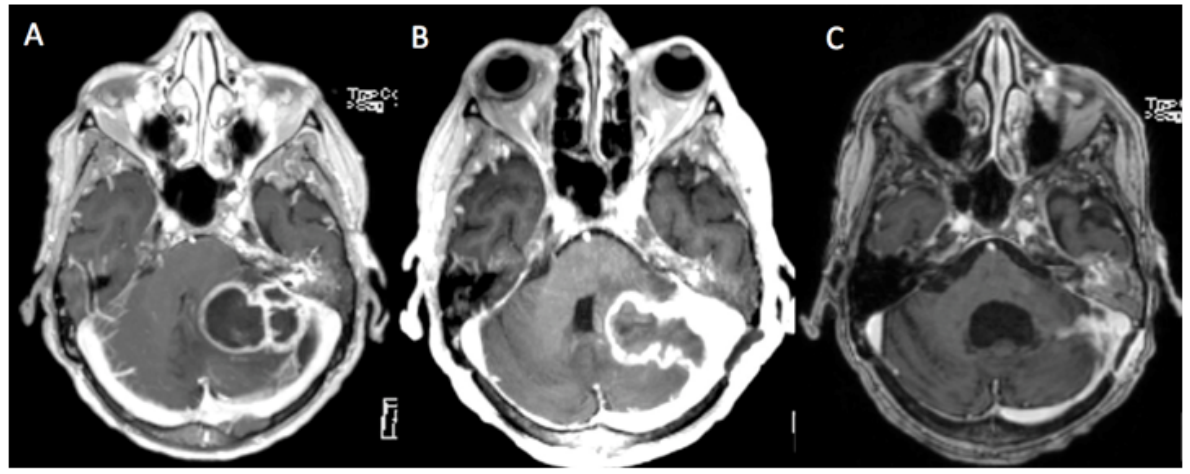

Figure 2: *A: Pre-operative MRI with contrast showing a large multilobulated abscess in the left cerebellopontine angle with severe compression of the left cerebellum and brain stem. There is also contrast-enhancement of the left pars petrosa and left internal acoustic meatus. B: MRI with contrast 19 days following surgery showing slight regression of the abscess and less compression of the posterior fossa. C: MRI with contrast 4 months following surgery showing almost absolved abscess and no compression of the elements in the posterior fossa.*

Patient case 3

A 72-year-old man, previously diagnosed with arterial hypertension and cerebral ischemic infarct, was admitted with symptoms of aphasia and left sided weakness. CT showed a frontal tumor close to the right motor cortex. The patient had no symptoms of infection.

However, due to rapid progression of the patients' neurological symptoms and a focal motor seizure a sub-acute MRI demonstrated growth of the tumor and differential weighted images indicated the tumor represented an abscess. The patient was acutely transferred to our neurosurgical unit and a burr hole and ultrasound guided puncture with drainage of 12 milliliters of pus was performed. Cultures from the pus had plentiful growth of *Campylobacter rectus*, *Streptococcus anginosus*, and *Fusobacterium nucleatum*, all sensitive to penicillin. The initial treatment of meropenem and ciprofloxacin along with metronidazole was changed to intravenous penicillin and metronidazole. Metronidazole was later discontinued due to side effects. The patient was suffering from aphasia and complete hemiparalysis of the left side, which slowly improved in the course of several weeks of antibiotics. The infection origin was determined to be a dental abscess and the patient had several teeth extracted and the infection site surgically debrided. However, after approximately 6 weeks of treatment the patient deteriorated neurologically, and a new MRI showed rupture of the frontal abscess into the right lateral ventricle and ventriculitis. An external ventricular drain was placed, and treatment was changed to intravenous meropenem, moxifloxacin, and metronidazole and intrathecal vancomycin. Cerebrospinal fluid cell count showed mild pleocytosis, however several cultures did not establish any bacterial growth. The patient slowly improved. Following a total of 12 weeks of antibiotic treatment the patient was discharged. The patient had a light left sided paresis and moved into a nursing home.

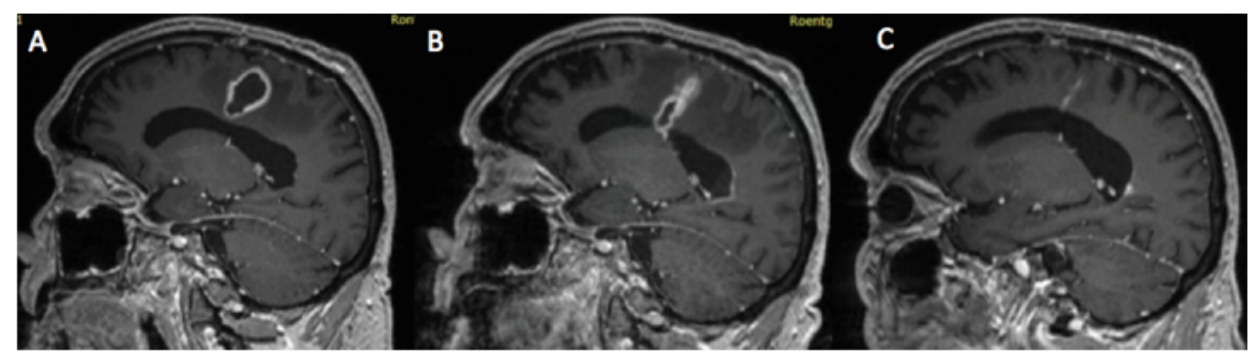

Figure 3: *A: Sagittal MRI with contrast showing abscess in the frontal lobe two days following surgical drainage. B: Sagittal MRI with contrast 6 weeks after start of treatment showing abscess rupture into the ventricle and contrast enhancing ependyma indicating ventriculitis. C: Sagittal MRI with contrast showing almost absolved abscess after 12 weeks of treatment.*

Patient case 4

A previously healthy 62-year-old woman was hospitalized following a week of fever and swelling of the right face and temporal region. Intravenous antibiotics was administered on suspicion of erysipelas. The patient sub-acutely developed a complete hemiparalysis and an acute CT and MRI showed subcutaneous abscess in the right temporal region with pathological signals along the underlying leptomeninges and minor subdural empyema. An acute craniectomy of the right temporal bone exposed an epi- and subdural empyema. Cultures from the subdural pus revealed a bacterial infection with *Campylobacter rectus*, *Staphylococcus epidermidis* and *Streptococcus anginosus*.

The infection originated from a tooth abscess and the patient subsequently had 5 teeth extracted. The patient was treated with intravenous penicillin, metronidazole, vancomycin, and azithromycin. Additional puncture of the empyema was performed 11 days after the initial operation. Due to renal dysfunction, the penicillin and vancomycin was discontinued, and treatment instead consisted of ceftriaxone and metronidazole. The patient's neurological deficits subsided along with a total of 6 weeks of antibiotics.

Case	Sex	Age	Symptoms	Focus	Bacteria	Antibiotics	Outcome
1	Male	42 y	Seizure Fever	Chronic peri-odontitis	*C. gracilis* *Fusobacterium*	Meropenem Metronidazole Fucidic acid	Full recovery
2	Female	71 y	Vomiting Headache Weight loss	Middle ear infection	*C. rectus* *F. nucleatum*	Meropenem Metronidazole	Bedridden with severe neuro-logical deficits
3	Male	72 y	Aphasia Left sided weakness	Dental abscess	*C. rectus* *F. nucleatum* *S. anginosa*	Meropenem Metronidazole Ciprofloxacin	Hemiparesis
4	Female	62 y	Fever Swelling face	Dental abscess	*C. rectus* *S anginosa* *S. epidermidis*	Penicillin Metronidazole Vancomycin Azithromycin	Full recovery

Table 1: *Summary of the four cases.*

Materials and Methods

The microbiology database

The microbiological database includes all samples investigated in the microbiology department since 2001.We reviewed all cases of Campylobacter species occurring in abscesses.

Literature search

We systematically searched Pubmed, Mendeley and PMC. Different search strings were used including "brain abscesses and *Campylobacter rectus*", "brain abscesses and *Campylobacter gracilis*" and "brain abscesses and *Campylobacter ureolyticus*". These strings were chosen to identify studies, which illuminate a possible association between brain abscesses and *Campylobacter* spp.

Database	Search string	Hits	Relevant hits	Studies
Pubmed	Brain abscesses and *Campylobacter rectus*	2	2	Martiny., *et al.* [5] De Vries., *et al.* [10]
	Brain abscesses and *Campylobacter gracilis*	1	1	De Vries., *et al.* [10]
	Brain abscesses and *Campylobacter ureolyticus*	0	0	
Mendeley	Brain abscesses and *Campylobacter rectus*	6	2	Martiny., *et al.* [5] De Vries., *et al.* [10]
	Brain abscesses and *Campylobacter gracilis*	3	1	De Vries., *et al.* [10]
	Brain abscesses and *Campylobacter rectus*	0	0	
PMC	Brain abscesses and *Campylobacter rectus*	100	5	Martiny., *et al.* [5] Marrie., *et al.* [6] Lam., *et al.* [9] Leo., *et al.* [11] Oka., *et al.* [12]
	Brain abscesses and *Campylobacter gracilis*	50	2	Marrie., *et al.* [6] Lam., *et al.* [9]
	Brain abscesses and *Campylobacter ureolyticus*	29	0	

Table 2: *The systematic search in following databases: PubMed, Mendeley and PMC.*

It is specified how many hits every search has given and how many of these hits, which were relevant to review.

For "brain abscesses and *Campylobacter rectus*" 2 hits were found in Pubmed, both were relevant, 6 hits were found in Mendeley, 2 of them were relevant, and 100 hits were found in PMC, 5 of them were relevant. For "brain abscesses and *Campylobacter gracilis*" 1 hit were found in PubMed and this was relevant, 3 hits were found in Mendeley and one of these was relevant and 50 hits were found in PMC were 5 of these were relevant. For "brain abscesses and *Campylobacter ureolyticus*" 0 hits were found in PubMed, 0 hits were found in Mendeley, and 29 hits were found in PMC, however none of them were relevant. This variation illustrates that these 3 databases differentiate from each other because of the different number of hits and the relevant number of studies. These 3 different search strings in the different databases were chosen for a wider selection in a specified search.

Results

Literature search

Table 3 summarizes the cases identified in our literature search. Four different *Campylobacter* spp. have been found in the studies, where *C. rectus* related to brain abscesses is the most occurring. Further other species such as *F. nucleatum* and *Eubacterium* spp. and others have been found in some of the studies. The mentioned *Campylobacter* spp. (*C. rectus, C. gracilis and C. concisus*) are typically found in the oral cavity.

Year	Author	Gender/ age	Material	Found A	Found B	Found C	Risk
2017	Martiny., et al.	Male/66	Brain abscess	*C. rectus*			Periodontitis Tooth abscess Otitis media
2008	De Vries., et al.	Female/35	Brain abscess	*C. gracilis*	*S. constellatus*	Anaerobic cooks	
		Male/65	Brain abscess	*C. concisus*			Maxillary sinus cancer
		Male/24	Spine	*C. rectus*	*Eubacterium spp.*	Actinomyces	
		Female/74	Abscess behind the eye	*C. Showae*	Micromonas		
2011	Lam., *et al*.	Female/41	Intracranial aneurism	*C. rectus*			
2014	Leo., *et al*.	Male/55	Sinus thrombosis	*C. rectus*			Tooth extraction
2018	Oka., *et al*.	Female/70	Sinus thrombosis	*F. nucleatum*	*C. rectus*		Tooth extraction
1990	Marrie., et al.	Female/62	Brain abscess	*W. recta (C. rectus)*	*S. intermedius*		

Table 3: *Results from literature search of brain abscesses with C. rectus, C. gracilis and C. ureolyticus. Text marked in bold and underlined fond marks studies containing cases of C. rectus in brain abscesses.*

The microbiology database

Campylobacter spp. in abscesses at Copenhagen University Hospital (Rigshospitalet) since 2001. As seen in table 4 *Campylobacter* spp. are found in several different kinds of abscesses and several *Campylobacter* spp. are represented.

Material	Department	Year	Found A	Found B	Found C
Brain abscess	Neurosurgery	2012	*C. gracilis*	*Fusobact.*	
Brain abscess	Neurosurgery	2011	*C. rectus*	*Fusobact.*	*S. anginosus*
Brain abscess	Neurosurgery	2020	*C. rectus*	*Fusobact.*	
Dura abscess	Neurosurgery	2021	*C. rectus*		
Brain abscess	Other hospital	2020	*C. rectus*		
Abscess behind ear	ENT	2020	*C. ureolyticus*		Skin flora
Abscess on neck	ENT	2020	*C. rectus*		
Thyreodea abscess	ICU	2018	*C. rectus*		*A. meyeri*
Abscess	Dental	2010	*C. gracilis*	*Fusobact.*	
Abscess	Gynecologi	2015	*Campylobacter* spp.		

Table 4: *Results from the hospital's microbiology database when searched of abscesses and Campylobacter spp.*

Interesting is the great proportion of brain abscesses with *Campylobacter* species and therefore this report concentrates on this type of abscesses.

Discussion and Conclusion

Several abscesses with *Campylobacter* spp., mainly *C. rectus,* were found within a short period of time. When looking into the microbiology database, four brain abscesses were found, which is the same number as described in the literature. This was a surprisingly high number.

C. rectus and *C. gracilis* are part of the oral microbiome, like *Fusobacterium* spp., which indicate that the brain abscesses may have an oral or an upper airway focus. This is in accordance with our findings, in which two patients have oral abscesses, one had periodontitis and one had a focus in the middle ear. A similar case was described by Martiny., *et al*. where the patient was previously diagnosed with a tooth abscess, periodontitis and otitis media [4]. Martiny., *et al*. proposed that these prior infections lead to spreading to the brain, causing the brain abscess [4]. Likewise was one case described by De Vries., *et al*. about a patient with a history of cancer in the maxillary sinus and later complications [5]. The study suggests that the brain abscess developed secondary to these complications [5].

The patients in our cases present a great variety of symptoms, often without any systemic signs of infection and brain abscess was not always obvious. *Campylobacter* spp. was often found together with *Fusobacterium* spp., and it could be a coincidence because they are both part of the oral microbiome or they may have a synergistic effect potentiating the pathogenesis of the infection. Most of the patients were treated with meropenem and metronidazole for 6 to 12 weeks. The two younger patients recovered completely, whereas the two elder patients continued to have chronic hemiparesis or neurological deficits.

Despite of the symptoms a brain abscess may always be suspected especially if there is a dental abscess, periodontitis, middle ear infection or sinusitis. When confirmed the brain abscess should have a broad antibiotic treatment for several months.

Even though it is a rare condition to have *Campylobacter* spp. in brain abscess, it may be of interest to look further into this as *C. rectus* and *C. gracilis* may be difficult to culture and may sometimes be overlooked.

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Conflict of Interest

The authors declare no conflict of interest or competing interest.

Informed Consent

All patients have given written consent to use the included data.

Code Availability and Ethics Approval

Not applicable not applicable for that section.

Authors Contribution

All authors have contributed to text and the revision of the text.

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