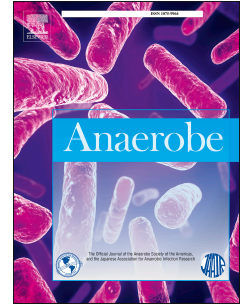


# Accepted Manuscript

Oesophageal pleural fistula presenting with *Parvimonas micra* infection causing cervical and brain abscesses

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1 **Oesophageal pleural fistula presenting with *Parvimonas micra* infection causing cervical**  
2 **and brain abscesses**

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**26 Abstract**

27 *Parvimonas micra* (*P. micra*) infections causing spinal cord compression are extremely rare.  
28 We report an occult oesophageal pleural fistula presenting with spinal epidural and brain  
29 abscesses resulting in severe neurological deficits caused by *P. micra*. Molecular detection  
30 proved to be instrumental in identifying the causative pathogen. Essential management with  
31 decompression, drainage, antibiotics and fistula repair lead to a good outcome.

**32 Key Words**

33 *Parvimonas micra*, abscess, spinal cord, fistula.

**34 Introduction**

35 Epidural abscesses are uncommon spinal infections. The cervical spine is the least common  
36 site in the neuraxis harbouring such infections and can be limb and/or life threatening [1].  
37 They often occur in high risk patients with HIV infection, intravenous drug abusers,  
38 diabetics, chronic renal failure patients and patients with malignancies [2]. Haematogenous  
39 spread from a distant focus is the usual mechanism of infection; however, contiguous  
40 dissemination is another possibility [3]. The main pathogen in spinal infections is  
41 *Staphylococcus aureus*, followed by coagulase-negative *Staphylococci*, and *Streptococci*;  
42 however anaerobic bacteria are relatively unusual pathogens [3]. *P. micra* is an anaerobic  
43 Gram-positive coccus [4] belonging to the common microflora of the oral cavity and  
44 gastrointestinal tract. It has been formerly known as *Micromonas micros* and  
45 *Peptostreptococcus micros* and was rarely implicated in spinal infections; however, a few  
46 cases have been reported in literature [5-12] including an intra-orbital and para-spinal  
47 infection [13].

48 We describe an unusual presentation of *P. micra* infection causing a cervical epidural abscess  
49 with spinal cord compression and neurological deficits along with multiple small intracranial  
50 abscesses in a patient with undiagnosed oesophageal pleural fistula. Urgent surgical

51 decompression, drainage of the epidural abscess, prolonged appropriate antibiotic regime and  
52 repair of the fistula improved the patient's outcome.

### 53 **Case Report**

54 A 65-year-old asthmatic male presented with a 1-week history of diarrhoea and vomiting,  
55 general weakness complained of neck pain 2 days prior to his presentation and developed a  
56 lower limb weakness a day before admission. His past medical history included a right  
57 pleurodesis and pleurectomy aged 17 for a recurrent pneumothorax.

58 His admission temperature was 38.9° C. His initial white blood cell count (WBC) was  
59 1520/mm<sup>3</sup> (Neutrophils 1310/mm<sup>3</sup>) and C-reactive protein (CRP) was 279 mg/dL. His  
60 symptoms progressed to include numbness, pins and needles in his lower and upper limbs,  
61 severe bilateral lower limb weakness (MRC grade 2-3), upper limb weakness (MRC grade 3-  
62 4) and urinary retention requiring catheterisation. CT scan at the referring hospital revealed a  
63 contrast enhancing epidural cervical collection consistent with an epidural abscess (Figure 1  
64 A&B). Intravenous (IV) ceftriaxone (2 g) and dexamethasone (8 mg) were administered  
65 immediately before transferring the patient to our neurosurgery unit. A neuraxis MRI  
66 revealed an extensive dorsal cervical epidural abscess with cord compression (Figure 1 C&D)  
67 and cerebral micro-abscesses in the posterior right cingulate cortex (Figure 2 A) with a tiny  
68 pocket of restricted diffusion and an infective focus in right corona radiata (Figure 2 B) as  
69 well as in the posterior left periventricular white matter. He underwent emergency cervical  
70 laminectomies (C3-7) and drainage of the epidural pus. The brain abscesses were small  
71 enough to be treated conservatively. Blood and pus samples were culture negative; gram-  
72 staining of the epidural pus showed large numbers of neutrophils, but no organisms were  
73 seen, therefore , a pus sample was sent to Great Ormond Street Hospital (GOSH) where  
74 broad-range 16S rDNA PCR analysis was performed as previously described [14, 15]. The  
75 pus sample was strongly positive in this assay and analysis of the resulting 320 base-pair

76 amplicon, that includes variable regions 1 and 2 of the 16S rRNA gene, was performed by  
77 BLAST searching against the Genbank database (<https://blast.ncbi.nlm.nih.gov>). The most  
78 closest related sequences were the 16S rDNA sequences from two *Parvimonas micra* type  
79 strains, with 99% sequence identity (Genbank accession numbers CP009761.1 and  
80 NR\_114338.1). This method is currently part of the routine clinical microbiology service at  
81 GOSH for the diagnosis of culture-negative infections [16]. The patient was started on a 6  
82 weeks course of IV ceftriaxone (2 g twice a day) and metronidazole (500 mg three times a  
83 day) initially which was extended to 12 weeks. Both antibiotics commenced in operating  
84 theatre just after draining the pus. Follow up brain imaging revealed the cerebral abscesses  
85 diminishing. An oral regime of antibiotics was not commenced after 6 weeks due to the  
86 surgical repair of the oesophageal-pleural fistula; therefore, he was continued on IV  
87 antibiotics for 12 weeks. Hepatitis B/C, HIV 1/2, and TB tests were negative. Transthoracic  
88 echocardiography was normal. Maxillofacial examination did not reveal any dental/sinus  
89 source of infection. Initial local CT was suspicious of right upper lobe lesion therefore; a  
90 contrast enhanced acquisition CT thorax with multi-planar reformats was performed and  
91 revealed a thick walled right-sided upper zone pleural based collection, which contains an air-  
92 fluid level (Figure 3 A, B, C). Within the superior mediastinum, the oesophagus was  
93 distended with air and there was a suspicion of a communication via a right outpouching to  
94 the pleural collection. Furthermore, a barium swallow demonstrated right-sided oesophageal-  
95 pleural fistula (Figure 3 D). The patient's inflammatory markers returned to normal levels, he  
96 continued to improve clinically with normal limb power and sensation on discharge followed  
97 by his fistula repair in a specialised centre 6 weeks after the initial presentation.

## 98 Discussion

99 *P. micra*, originally *Peptostreptococcus micros* but was reclassified and gained its name  
100 recently [17], is a strongly proteolytic anaerobic species that is increasingly known as an

101 important pathogen in oral infections, particularly periodontitis, and mixed anaerobic deep-  
102 organ abscesses [18]. Spinal infections are uncommon and only represent about 2-4% of bone  
103 infections [1]. Spondylodiscitis caused by anaerobic bacteria remain a rare subgroup and  
104 represent only 3-4% of all bacteria isolated from such infections [6, 10]. We report a life  
105 threatening but treatable cervical epidural abscess and concurrent brain abscesses, in an  
106 otherwise healthy individual. The cause of this infection is a rare anaerobic microorganism in  
107 a patient with underlying oesophageal pleural fistula. *P. micra* has been described in a few  
108 case reports of mostly spondylodiscitis alone or rarely with associated epidural abscess [5, 6,  
109 8-11, 19]. Our patient clinical presentation was different from the previously reported cases  
110 and was not associated with spondylodiscitis as in the reported cases to date. Furthermore, the  
111 development of neurological symptoms and subsequent deterioration occurred in a matter of  
112 days. However, in agreement with the literature, he presented with an inflammatory  
113 syndrome and deterioration in health [8]. Given that *P. micra* is an oral cavity and  
114 gastrointestinal tract microflora [4], the most likely source for the *P. micra* infection causing  
115 the cervical epidural abscess in our case is the undiagnosed oesophageal pleural fistula.  
116 However, the brain abscesses are likely caused by haematogenous spread and this theory is  
117 supported by a previous report of meningitis, at least in part, due to *P. micra* infection [11].  
118 To our knowledge, *P. micra* resulting in brain abscess is extremely rare which has been  
119 described only in one case and in combination with a streptococcal orbital infection [20]. An  
120 oesophageal pleural fistula is an uncommon condition and can be caused by instrumentation,  
121 malignancy, surgery or a post-pneumectomy complication [21]. Our patient underwent a  
122 pleurectomy four decades ago and this is likely the cause of his fistula. Importantly, these  
123 fistulae are associated with high morbidity and mortality because of ensuing empyema and  
124 nutritional debilitation [22]. Given the previous, we suspect that morbidity is higher and  
125 prognosis is worse in a patient with such fistula accompanied with spinal and cranial

126 infections causing severe neurological deficits. However, we can report a steady  
127 improvement after cervical decompression, abscess drainage and antibiotic treatment in  
128 accordance with previously proposed recent treatment strategies [7]. *P. micra* as an anaerobic  
129 organism causing epidural abscesses and/or other infections may be difficult to culture [23].  
130 Pus and blood cultures were negative in our case. In addition to the usual difficulties in  
131 isolating *P. micra*, our patient received a pre-operative dose of ceftriaxone and this may have  
132 had an impact on the culture results. The diagnosis of epidural abscess caused by *P. micra*  
133 was only possible by performing broad-range 16S rDNA PCR and sequencing [16]. This  
134 method has recently played an important role in the accurate identification of bacterial  
135 isolates and the discovery of novel bacteria in clinical settings when the conventional culture  
136 methods failed to identify the pathogen [14, 15, 23]. Therefore, we believe 16S rDNA PCR  
137 and sequencing is essential method for bacterial pathogen detection and identification for  
138 patients who had received antibiotics prior to obtaining pus samples. Our patient received  
139 metronidazole and ceftriaxone (due to intracranial involvement) with a planned 6 weeks  
140 course of intravenous antibiotics however; this was extended to 12 weeks due to the surgical  
141 repair of the fistula. Immediate neurological improvement was noted and the patient  
142 continued to improve and walked out of the department after 3 weeks to his local hospital to  
143 continue IV antibiotics and definitive gastroenterology treatment. A trial of conservative  
144 management (nasogastric feed only) failed to obliterate the fistula and surgical repair 6 weeks  
145 after his initial presentation was required.

146 In conclusion, this is the first confirmed case of a severe *P. micra* infection causing a cervical  
147 epidural abscess with brain abscesses but without spondylodiscitis, secondary to an  
148 oesophageal pleural fistula. The present report indicates that molecular technologies namely  
149 16S rDNA PCR and sequencing have a proven and instrumental role in identifying the  
150 causative bacterial pathogen particularly when diagnostic samples can only be obtained after

151 commencement of antibiotic therapy. Prompt decompression and drainage of the abscess  
152 causing neurological deficit with diagnosis and treatment of the source resulted in desirable  
153 outcome.

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209

## 210 **Figure Legends**

211 **Figure 1** Pre-operative images. A Post contrast sagittal CT image reveals an epidural  
212 enhanced collection between C2-6 (arrow). B Post contrast axial CT image at C4 level  
213 showing the epidural abscess (arrow). C Post GAD T1W sagittal image demonstrating an  
214 enhanced epidural abscess extending from C2 to T1 (arrow). D Post GAD axial T1W image  
215 at C4 revealing the enhanced epidural abscess with spinal cord compression (arrow).

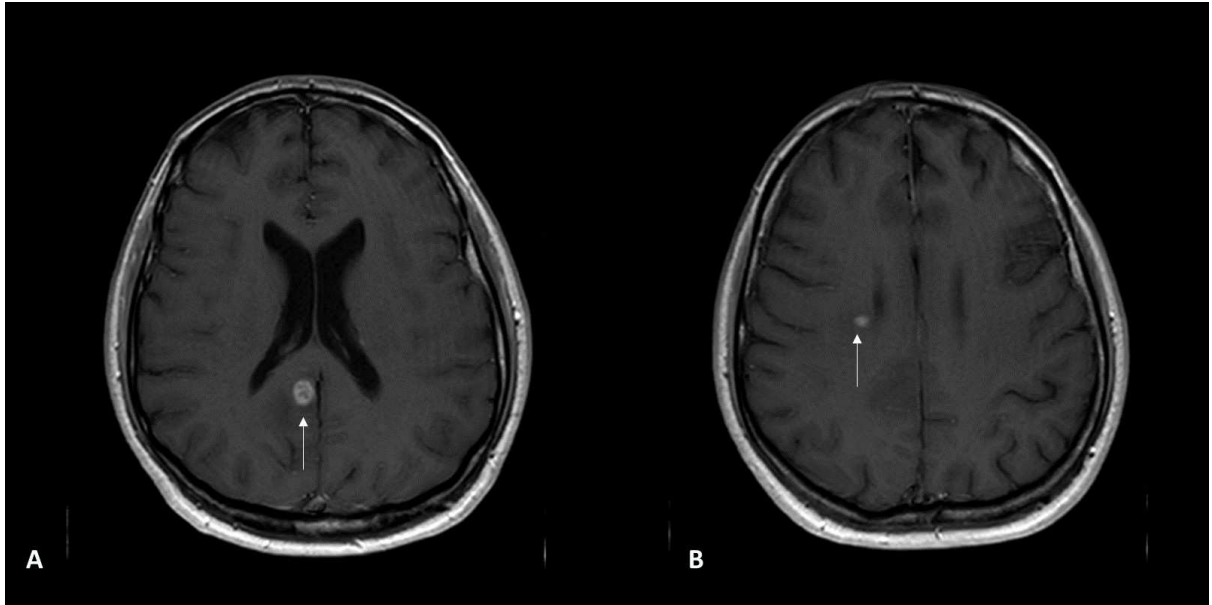
216 **Figure 2** MRI Brain. A Post GAD axial T1W image demonstrating a small rounded thick  
217 walled lesion centred on the posterior right cingulate cortex (arrow). B Post GAD axial T1W  
218 image showing a smaller enhancing lesion in the right corona radiata (arrow).

219 **Figure 3** Contrast enhanced acquisition CT thorax with multi-planar reformats. Post contrast  
220 A axial CT, B coronal CT and C Sagittal CT demonstrating a right-sided thick-walled pleural  
221 collection with an air fluid level and a probable fistulous communication with the oesophagus  
222 (arrows). D A barium swallow revealing the oesophageal pleural fistula (arrow).

223



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**Highlights:**

- *P. micra* causing serious spinal epidural and brain abscesses.
- Broad-range 16S rDNA PCR analysis is an essential diagnostic tool.
- Oesophageal pleural fistula as infection route.