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Capnocytophaga canimorsus Meningoencephalitis Diagnosed by PCR-Free Shotgun Metagenomics of CSF with Read-Level blaOXA-347 Detection: A Case Report

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Abstract

Background

Capnocytophaga canimorsus is a fastidious canine oral commensal bacterium and an uncommon cause of severe invasive infection. It grows slowly, thus invasive disease can be frequently culture-negative, and is absent from licensed panels making it difficult to be identified as cause of sepsis and meningoencephalitis. This case-based review asks when it should be suspected in a critically ill patient, how PCR-free metagenomic sequencing can help diagnosis in complicated settings and how much weight antimicrobial-resistance results from metagenomic sequencing should carry.

Methods

We describe a case of culture-negative *C. canimorsus* meningoencephalitis managed in our intensive care unit, in which cerebrospinal fluid (CSF) metagenomic sequencing was pivotal for diagnostic and for proper antibiotic stewardship. To contextualise it we reviewed the literature on invasive *C. canimorsus* infection and screened 45 public genomes for class-D β-lactamases.

Results

A 60-year-old man with alcohol-related liver disease and a household dog, but no bite, presented with seizure and coma. CSF was frankly inflammatory, yet two multiplex panels were negative, a pneumococcal antigen test was falsely positive and cultures were sterile at 48 h. On day 5 of hospitalization, PCR-free metagenomic sequencing of CSF identified *C. canimorsus* as the dominant organism responsible of infection. Read-level resistance screening of the same data returned two reads assigned to *bla*OXA-347, and standard ampicillin therapy was replaced by doxycycline. The organism was later recovered on extended culture, identification being reported on day 18. Among 45 public genomes of *C. canimorsus* analyzed, only four carried a class-D β-lactamase.

Conclusions

Metagenomic sequencing identified a fastidious pathogen thirteen days before the gold-standard culture-based identification. This case supports inclusion of CSF shotgun mNGS, combined with read-mapping-based resistome screening, in the diagnostic algorithm for culture-negative, syndromic-PCR-negative community-acquired bacterial meningitis.

Background

Capnocytophaga canimorsus is a capnophilic Gram-negative bacillus carried in the oral flora of most dogs and many cats [1]. Human infection is rare, but severe, at roughly 0.5–0.7 cases per million per year in surveillance of few northern European countries [2, 3]. Splenectomy and alcohol misuse dominate the published risk profile [4, 5, 6], and in a public-health reference-laboratory series 45% of patients had at least one immune-compromising condition [5, 6, 7]. Sepsis dominates the clinical spectrum: in a French multicentre series of 44 zoonotic *Capnocytophaga* infections, of which 41 were *C. canimorsus*, sepsis accounted for 84% of cases and meningitis for 18% [6].

Three factors converge to make culture- and PCR-based diagnosis of this pathogen unreliable: (i) the organism requires CO_2-enriched media and 2–7 days minimum of incubation to yield visible colonies; (ii) it is not a target of any FDA- or CE-IVD-approved meningoencephalitis (ME) panel; and (iii) prior empirical β-lactam therapy can suppress culture recovery [8, 9]. Unbiased metagenomic next-generation sequencing (mNGS) of CSF to identify pathogens is becoming more and more central in hospital diagnosis [10] and can be used to close exactly this kind of gap also for the identification of *C. canimorsus* [11].

Case report

A 60-year-old seasonal worker was found by relatives stuporous, incontinent and soiled with vomit. He had long-standing heavy alcohol use, untreated hepatitis C infection and hypertension, and was unvaccinated against *Streptococcus pneumoniae*. He lived alone with a household dog. There had been **no bite, scratch or other breach of the skin**; contact was ordinary cohabitation. He had sustained a minor head injury after a garden fall several days earlier, thus the primary concern was to exclude a possible intracranial bleed.

Emergency services recorded a Glasgow Coma Scale of 9. During helicopter transfer he had a generalised tonic-clonic seizure and was intubated. On arrival he was acidotic (pH 7.17) and hyperlactataemic (8.7 mmol/L), with leucocytosis (26.6 × 10^9/L) and procalcitonin 9.28 ng/mL; blood ethanol was undetectable (Table 1). Cranial computed tomography and CT-angiography excluded haemorrhage and large-vessel occlusion.

Table 1
Biochemical parameters at admission

Parameter at admission	Result	Reference range	Interpretation
Arterial blood gas	FiO_2 0.45	-	-
	pH 7.172	pH 7.35–7.45	Low
	pCO2 55.1 mmHg	pCO2 36–40 mmHg	Elevated
	pO2 161 mmHg	pO2 83–108 mmHg	Elevated
	PaO_2/FiO_2 359 mmHg	PaO_2/FiO_2 >300 mmHg	Near normal
Glucose	5 mg/dL	70–99 mg/dL	Low
Lactate	8.7 mmol/L	0.5–2.2 mmol/L	High
Base excess	−7.7 mmol/L	-2 / +2 mmol/L	Metabolic acidosis
White-cell count	26.6 × 10^9/L	5–10 × 10^9/L	Leukocytosis
C-reactive protein	37.4 mg/L	0.06-10 mg/L	Elevated
Procalcitonin	9.28 ng/mL	-	High Risk of Sepsis / Shock
Blood ethanol	< 0.03 g/L	0.05 g/L	No blood alcohol detected

Given nuchal rigidity and his unvaccinated status, lumbar puncture was performed. CSF was xanthochromic and frankly inflammatory: 413 cells/μL with 60% neutrophils, protein 581 mg/dL, glucose 5 mg/dL (CSF/serum ratio 0.03) and lactate 18 mmol/L (Table 2). Gram stain showed rare slender Gram-negative-to-variable bacilli that could not be assigned. Considering these results, intravenous ceftriaxone, ampicillin and aciclovir were started in accordance with European guidance [12]; aciclovir was included because of a herpetic labial lesion.

Table 2
Cerebrospinal fluid and ancillary microbiology results on admission (hospital day 0)

Parameter	Result	Reference range	Interpretation
Appearance	Sublimpid, slightly xanthochromic	Limpid, colourless	Abnormal
Cell count	413 cells/μL	< 5 cells/μL	Marked pleocytosis
Differential	60% neutrophils, 40% lymphocytes	—	Neutrophil-predominant
Total protein	581 mg/dL	15–45 mg/dL	Markedly elevated
Glucose	5 mg/dL	40–70 mg/dL	Severely depressed
CSF/serum glucose ratio	0.03	> 0.6	Critically low
Lactate	18 mmol/L	1.1–2.4 mmol/L	Markedly elevated
Gram stain	Rare Gram-negative/variable bacilli	Negative	Suggestive of bacterial meningitis
ANCILLARY RESULTS	**Result**		**Interpretation**
QIAstat-Dx® ME panel	Negative for all 14 targets	—	Non-diagnostic
BioFire® FilmArray® ME 2.0 panel	Negative for all 43 targets	—	Non-diagnostic
Pneumococcal antigen (CSF, urine)	Positive	—	Reclassified as false positive
Routine CSF culture (48 h)	Sterile	—	Non-diagnostic (eventually positive on prolonged incubation)
Blood culture (48 h)	Sterile	—	Non-diagnostic
Serology for HIV (day 2)	Negative	—	No infection
Serology for HBV (day 2)	Negative	—	No infection
Serology for Borrelia (day 2)	Negative	—	No infection
Serology for TBE (day 2)	Negative	—	No infection
Serology for HCV (day 2)	Positive	—	Positive (confirmation of patient history)
Plasma HCV-RNA (day 2)	357,997 IU/mL	< 15 IU/mL	Active HCV viraemia
Tracheal aspirate (day 1)	Bordetella bronchiseptica > 10^5 CFU/mL	Sterile	Probable airway colonisation

ME, meningoencephalitis. The 14 targets of the QIAstat-Dx® panel include Escherichia coli K1, *Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus pneumoniae, S. agalactiae, S. pyogenes, Mycoplasma pneumoniae*, enterovirus, HSV-1/2, HHV-6, parechovirus, VZV, and *Cryptococcus neoformans/gattii.* The BioFire® FilmArray® ME 2.0 panel was used off-label and tested 43 cumulative bacterial, viral and fungal targets. *Borrelia* and tick-borne encephalitis virus (TBE) serology testing was included because the patient lived in an area endemic for ticks that carry these pathogens.

The workup then became actively misleading (Fig. 1). Rapid pneumococcal antigen was positive in both urine and CSF, yet syndromic molecular testing was negative for all 14 targets of each of two panels; the antigen result was reinterpreted as a false positive. An oral-lesion swab was positive for HSV-1, however there was no evidence of CNS involvement due to the previous syndromic panel testing. On day 2, serologic testing was performed. HCV serology was confirmed positive with active viremia (consistent with patient history), while all the other serology were negative (Table 2). Blood and CSF cultures were sterile at 48 h. A tracheal aspirate grew *Bordetella bronchiseptica* at > 10^5 CFU/mL — another canine organism- which briefly appeared a plausible aetiology [13]. Contrast-enhanced magnetic resonance imaging on day 5 demonstrated leptomeningeal enhancement, cerebral microhaemorrhages and restricted diffusion within the occipital horns and fourth ventricle, consistent with meningoencephalitis and purulent ventriculitis (Fig. 2).

With sterile cultures, both panels negative and the only positive result inconsistent with them, residual day-0 CSF underwent PCR-free shotgun mNGS. Of 6,337,254 reads, 3,121 were bacterial. *Capnocytophaga spp*. accounted for 3,052 of these (97.8%), of which 2,618 (85.8% of the genus reads) were assigned to *C. canimorsus*; *Bordetella* accounted for 5 reads (0.16%). The result was communicated on day 5 of patient hospitalization (Fig. 1). Assembly-based resistance screening was performed but didn't give any meaningful result. Resistance Gene Identifier of the Comprehensive Antibiotic Resistance Database (CARD) was then used to perform read-level screening in read-mapping mode [14] and this returned two unpaired reads assigned to *bla*OXA-347, a class-D β-lactamase described in animal-bite-associated *Capnocytophaga* [15]. This finding alongside a published report of ceftriaxone failure in *C. canimorsus* meningitis [16], was deemed sufficient evidence to switch therapy: ampicillin was stopped on day 5 and doxycycline added for seven days to provide non-β-lactam cover.

Ceftriaxone ran from day 0 to day 19, briefly paused on day 5 and resumed on day 6 after a febrile relapse. The course was complicated by ventilator-associated pneumonia with AmpC-derepressed *Enterobacter cloacae*, treated with meropenem (Fig. 1) — a recognised consequence of third-generation cephalosporin exposure [16]. He was extubated on day 9, transferred to rehabilitation on day 11, walked independently by day 22 and was discharged on day 27. Hepatitis C was subsequently cured, and at eight months he was asymptomatic, ambulant and abstinent from alcohol.

The CSF culture, held for extended incubation, ultimately grew *C. canimorsus*; identification was reported on day 18, thirteen days after the metagenomic result (Fig. 1).

Discussion and case-based literature review

Usually, *C. canimorsus* case reports are written about memorable bites, whereas our case belongs to a larger, quieter group. Pooled case-report reviews record a dog bite in 54–60% of *C. canimorsus* infections [4, 5], and this has hardened into a clinical rule of thumb. Laboratory-ascertained series say otherwise. A Californian reference-laboratory review found a bite in only 14% of patients infected with zoonotic *Capnocytophaga* species [7]; in a Helsinki series of 65 patients with *C. canimorsus* bacteraemia every patient had had contact with a dog but only 37% had been bitten, leading those authors to conclude that a dog in the household may be sufficient exposure for severe disease [17]. In one systematic review of *C. canimorsus* meningitis, 11% of patients reported no animal contact at all [8], and meningitis with bacteraemia has been described in an immunocompetent adult without any bite [9]. Clinicians should always bear this caveat in mind: a bite history is a reason to think of *Capnocytophaga*; its absence is not a reason to dismiss as a potential etiological agent.

Diagnostic Challenges in *Capnocytophaga canimorsus* infection

This case recapitulates several well-documented pitfalls in the diagnosis of *C. canimorsus* CNS infection. Despite a profoundly inflammatory CSF profile, routine culture and two independent multiplex syndromic panels returned negative results within the actionable diagnostic window. Culture was slow rather than negative — it did grow the organism, but the identification arrived on day 18, by which time the patient had left intensive care. This is a common problem: across published cases of *C. canimorsus* meningitis, CSF cultures are positive in about 70% at a median of five days and blood cultures in 54% at a median of four days [8]. In our case, this delay led to other hypothesis: a canine commensal/pathogen (*B. bronchiseptica*) recovered from the airway introduced an attractive but ultimately misleading etiological candidate, and the rapid pneumococcal antigen test generated a result that briefly directed therapy toward the wrong organism. Furthermore, the clinical suspicion of HSV encephalitis—which can occasionally yield false-negative results on early CSF testing—served yet another diagnostic distractor. Cumulatively, these findings exemplify the diagnostic ambiguity that justifies CSF mNGS as a second-tier, hypothesis-free test [10, 11, 18, 19].

From Diagnostic Ambiguity to Etiological Confirmation: The Added Value of CSF mNGS

The PCR-free shotgun mNGS workflow recovered enough *C. canimorsus* sequence on a low-biomass CSF specimen (~ 1.1 Mb, ~ 30% breadth of reference) to provide an unambiguous etiological ranking: *C. canimorsus* represented 84.0% of the 3,121 bacterial reads, compared with 0.16% for *Bordetella* spp. (Fig. 3**)**.

The signal-to-noise advantage of PCR-free over amplification-based libraries was helpful: PCR amplification would have distorted relative read distributions and hindered the discrimination between a CNS pathogen and an airway coloniser present at low DNA mass [20]. The several-hundred-fold separation between *Capnocytophaga* and the airway coloniser *Bordetella* could be interpreted as a real difference in burden rather than an amplification artefact — precisely the discrimination this case required.

The five-day interval from sample collection to actionable result was set by batched-run scheduling in our diagnostic workflow rather than by intrinsic biochemistry; rapid implementations using long-read platforms (Oxford Nanopore) with wet-lab host depletion have demonstrated time-to-result of < 16 h [20] and represent the next iteration of the technique.

The novel diagnostic insight in this case derived not only from the assembled metagenome but from re-screening of the unassembled reads with CARD/RGI in BWT mode, which recovered two unpaired reads mapping to *bla*OXA-347. Assembly-first AMR pipelines (ABRicate, AMRFinderPlus, VFDB, CARD-BLAST) returned no resistance signal because the affected locus was below the assembly threshold. A read-mapping approach is therefore informative for the retrieval of low-abundance resistance markers in clinical mNGS data; a two-read positivity signal is of limited specificity in isolation, but in the context of the genus-specific epidemiology of OXA-347 acquires substantial clinical plausibility.

This case highlights how ultra-sensitive read-mapping can recover resistance signals below assembly thresholds while their clinical significance remains context-dependent, supporting the need for interpretative frameworks rather than simplistic present/absent resistance reporting.

OXA-347 was first characterised by Zangenah et al. [15] in animal-bite-associated *Capnocytophaga* (predominantly *C. cynodegmi* and *C. canimorsus*) as a class-D β-lactamase with broad substrate specificity including penicillin and, variably, cephalosporins. Despite elevated imipenem MICs in some heterologous expression systems, it is not a clinically meaningful carbapenemase in *Capnocytophaga* [15, 21]. Recent surveillance by Umeda et al. [22] confirmed *bla*OXA-347 in *C. canimorsus* and *C. canis* isolates from companion animals with elevated phenotypic MICs to penicillin,

ceftriaxone and cefepime and consistently low MICs to imipenem and amoxicillin/clavulanate. Wildman et al. [16] reported a clinical *C. canimorsus* meningitis case in which ceftriaxone monotherapy initially appeared effective but lead to clinical failure requiring meropenem escalation; that isolate also failed to grow sufficiently for formal AST — exactly the scenario in which a read-level resistome signal from mNGS is most decisive.

Core-Genome Phylogeny of *Capnocytophaga canimorsus*

A core-genome maximum-likelihood phylogeny was reconstructed for *C. canimorsus*, including the case isolate, 45 publicly available *C. canimorsus* genomes, and three *C. cynodegmi* genomes used as the outgroup to root the tree (Fig. 5).

The phylogeny was inferred from a concatenated alignment of 291 core genes, comprising 323,613 nucleotide positions. Branch lengths represent the estimated number of substitutions per site. The placement of the case isolate within the *C. canimorsus* population is highlighted. The isolate was placed in close phylogenetic proximity to three *C. canimorsus* genomes harboring *bla*OXA-347, indicating a high degree of genomic relatedness. This result corroborates our finding of *bla*OXA-347 reads, even if in a very small amount, however, is not sufficient to confirm a phenotype of resistance.

Place in literature

A focused literature search (PubMed and Google Scholar, 2021–2025, terms "*Capnocytophaga canimorsus*" AND "meningitis") identified 14 PubMed-indexed case reports for comparison, summarised in Table 3 and visualised in Fig. 4.

Table 3
Recent (2021–2025) reported cases of Capnocytophaga canimorsus meningitis — focused literature review

Reference (year)	Age / Sex	Comorbidity / risk factor	Animal exposure	Blood culture	CSF WBC (cells/ µL)	CSF protein (mg/dL)	Treatment	Outcome
Germuskova 2025 [28]	Late 50s / M	Alcohol overuse	Dog bite, 1 wk prior	+	9 000	52.1	Meropenem + broad spectrum	Died < 12 h
Fort 2026 [30]	27 / M	None reported	None	+	NR	NR	Post-mortem diagnosis	Died
Tao 2025 [29]	76 / M	Immunocompromised	None	+	2 374 (94% PMN)	223	Empirical → meropenem	Discharged at 4 wk
Wildman 2024 [16]	70 / F	Smoker	Dog bite	– ; CSF +	699 (95% PMN)	128	Ceftriaxone → meropenem after CRO failure	Discharged day 16
De Rosa 2024 [23]	48 / M	Splenectomy; β-thalassaemia; cirrhosis; DM	Dog bite	+	1 739 (92.5% PMN)	421.6	Meropenem → ceftriaxone; ECBP	Recovered
Grewal 2024 [25]	74 / F	Hypertension, hypothyroidism	Dog bite	+	1 487	747	Meropenem → amoxicillin/clavulanate	Improved
van der Hoeven 2024 [24]	46 / M	Smoker; heavy alcohol use	Camping with dog	– ; CSF +	2 160	206.2	Amoxicillin + ceftriaxone (7 d)	Recovery
Tang 2024 [31]	84 / M	Prednisone; cardiac comorbidities	Puppy lick (open wound)	+	7 336 (82% PMN)	897	Meropenem	Discharged
Lam 2023 [27]	32 / F	Healthy	Occupational (veterinarian)	–	1 830 (75% PMN)	140	Ceftriaxone	Asymptomatic at 6 mo
Villar 2023 [26]	38 / F	Immunocompetent	Scratch / lick	+	4 612 (79% PMN)	348	Ceftriaxone + steroids	Residual hearing loss
Fennell 2022 [32]	38 / F	Healthy	Scratch / lick	+	NR	NR	Antibiotics + steroids	Discharged
Farias 2022 [33]	85 / M	COVID-19	Dog bite, 15 d prior	–	727 (89% PMN)	171.3	Ceftriaxone → meropenem	Full recovery at 6 mo
Asif 2021 [34]	55 / F	Multiple comorbidities	Dog bite, 2 d prior	–	4 000 (90% PMN)	79.7	Vancomycin + ceftriaxone → CRO 3 wk	Full recovery
O'Riordan 2021 [9]	60 / F	Immunocompetent	Cat exposure	– ; CSF +	NR	NR	Ceftriaxone	Recovered
Hansen 2019 [8] (pooled)	Various	Various	Various	Various	Various	Various	Mixed CRO/meropenem	~ 76% survival across literature
Present case (2025/26)	**60 / M**	**Heavy alcohol use; HCV F4 cirrhosis**	**Household dog (no bite)**	**Sterile during workup**	**413 (60% PMN)**	**581**	Ceftriaxone + doxycycline (mNGS-guided); meropenem for E. cloacae* VAP**	**Full neurological recovery; HCV cured**

Abbreviations: CRO, ceftriaxone; CSF, cerebrospinal fluid; DM, diabetes mellitus; ECBP, extracorporeal blood purification; mNGS, metagenomic next-generation sequencing; NR, not reported; PMN, polymorphonuclear cells; VAP, ventilator-associated pneumonia; WBC, white-cell count; +, positive; –, negative.

Across these reports and the present case (n = 15), mean age was 57 years (range 27–85), 53% of patients were male, and 80% had documented animal exposure (most commonly dog bite, occasionally lick or scratch); about two thirds had at least one comorbidity (alcohol overuse, splenectomy, cirrhosis, diabetes mellitus, COVID-19, smoking or immunosuppressive therapy). CSF profiles were uniformly inflammatory with neutrophil-predominant pleocytosis (median ~ 1,500 cells/µL), markedly elevated protein and depressed glucose. Blood cultures were positive in 9/15 (60%) published cases. Treatment regimens almost universally included a third-generation cephalosporin and/or meropenem, often with empirical-to-targeted de-escalation after culture or genomic identification [23, 24, 25]. Two of 15 published cases (13%) were fatal, and

approximately one third of survivors had documented residual neurological deficits, particularly sensorineural hearing loss [26] and gait abnormalities (our case).

Recovery of the pathogen varies greatly between the 15 reports found in literature. Only one case states to have used multiplex PCR for primary diagnosis [8] and other two used 16s rRNA PCR on the patient's CSF sample respectively for a primary identification and a secondary confirmation after MALDI-TOF identification [9, 27]. Germuskova's study was on strains already identified as *Capnocytophaga canimorsus* [28]. Most of the cases showed CSF or blood (or both) culture growth and consequently identification of the pathogen with MALDI-TOF MS analysis from: MALDI-TOF MS analysis of the CSF cultures happened in 8 cases [16, 24, 26, 29, 30, 31, 32, 33] and from blood cultures in other 8 cases [9, 23, 25, 26, 29, 30, 31, 32], three of which identified the pathogen on both matrixes. Another case used next-generation sequencing, but differently from our case they analysed the blood sample [34, 35].To our knowledge, the present case is the first to combine (i) PCR-free shotgun mNGS of CSF, (ii) read-level CARD/RGI BWT resistome screening yielding *bla*OXA-347 prior to phenotypic confirmation, (iii) prospective therapy modification on that basis, and (iv) full clinical recovery despite intercurrent AmpC-derepressed *E. cloacae* VAP and underlying HCV-related cirrhosis subsequently cured.

Limitations

This report is subject to the limitations intrinsic to a single-patient case. The *bla*OXA-347 detection rested on two unpaired reads only and therefore has limited specificity in isolation; orthogonal confirmation by re-sequencing was attempted but was inconclusive owing to insufficient DNA biomass, and phenotypic AST could not be performed. Read-level signals at this low abundance remain susceptible to index-hopping and low-frequency "kitome" contamination, although the parallel negative controls were clean and the genus-specific epidemiology of OXA-347 supports clinical plausibility. The mNGS workflow was wet-lab batched and required approximately 36 hours from specimen receipt to result; rapid Nanopore-based protocols offer substantially faster turnaround but were not available at our institution at the time of the case.

Conclusion

Unbiased metagenomic sequencing of CSF identified a fastidious pathogen almost two weeks before the culture-based identification, while every conventional test had failed or misled the clinicians. PCR-free shotgun metagenomic sequencing of CSF, complemented by read-mapping-based resistome screening on the unassembled raw reads, can provide unambiguous etiological identification and a hypothesis-generating resistome signal — including for class-D β-lactamases such as OXA-347 in *Capnocytophaga* — in culture-negative, syndromic-PCR-negative bacterial meningoencephalitis. Clinically integrated mNGS, with combined assembly- and read-mapping-based AMR analysis and explicit attention to genus-specific resistome epidemiology, merits prospective evaluation as a second-tier test in this setting when all other conventional test is failing. It should be noted that is important to pursue prolonged culture to recover this organism, because the isolate remains the only source for phenotypic AST evaluation.

Abbreviations

AmpC	Ampler C β-lactamase
ANI	Average nucleotide identity
CARD	Comprehensive Antibiotic Resistance Database
CFU	Colony-forming units
CSF	Cerebrospinal fluid
CT	Computed tomography
DNA	Deoxyribonucleic acid
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FLAIR	Fluid-attenuated inversion recovery
ICU	Intensive care unit
MIC	Minimum inhibitory concentration
mNGS	Metagenomic next-generation sequencing
MRI	Magnetic resonance imaging
PCR	Polymerase chain reaction
SH-aLRT	Shimodaira-Hasegawa approximate likelihood-ratio test

Declarations

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Author contributions

GL and FB designed the study. GL, MB, FB, MC and GMo provided clinical care and collected the clinical data. MC, GBe, MS, PF, BZP and CSC performed the laboratory investigations. GL performed the bioinformatic and phylogenomic analyses and drafted the manuscript. CS and GBa supervised the work. All authors revised the manuscript critically for important intellectual content, and read and approved the final version.

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Data availability

De-identified clinical data and the host-depleted cerebrospinal fluid read set are available from the corresponding author on reasonable request; raw reads contain residual host DNA and cannot be deposited without access restriction.

Ethics approval and consent to participate

According to local regulations (Comitato Etico per la Sperimentazione Clinica della Provincia di Trento), formal ethics-committee approval is not required for publication of a single-patient anonymised report. The work was conducted in accordance with the Declaration of Helsinki and is reported in accordance with the CARE guidelines.

Consent for publication

Written informed consent for publication of the clinical details and accompanying images was obtained from the patient.

Competing interests

The authors declare no competing interests.

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Figures

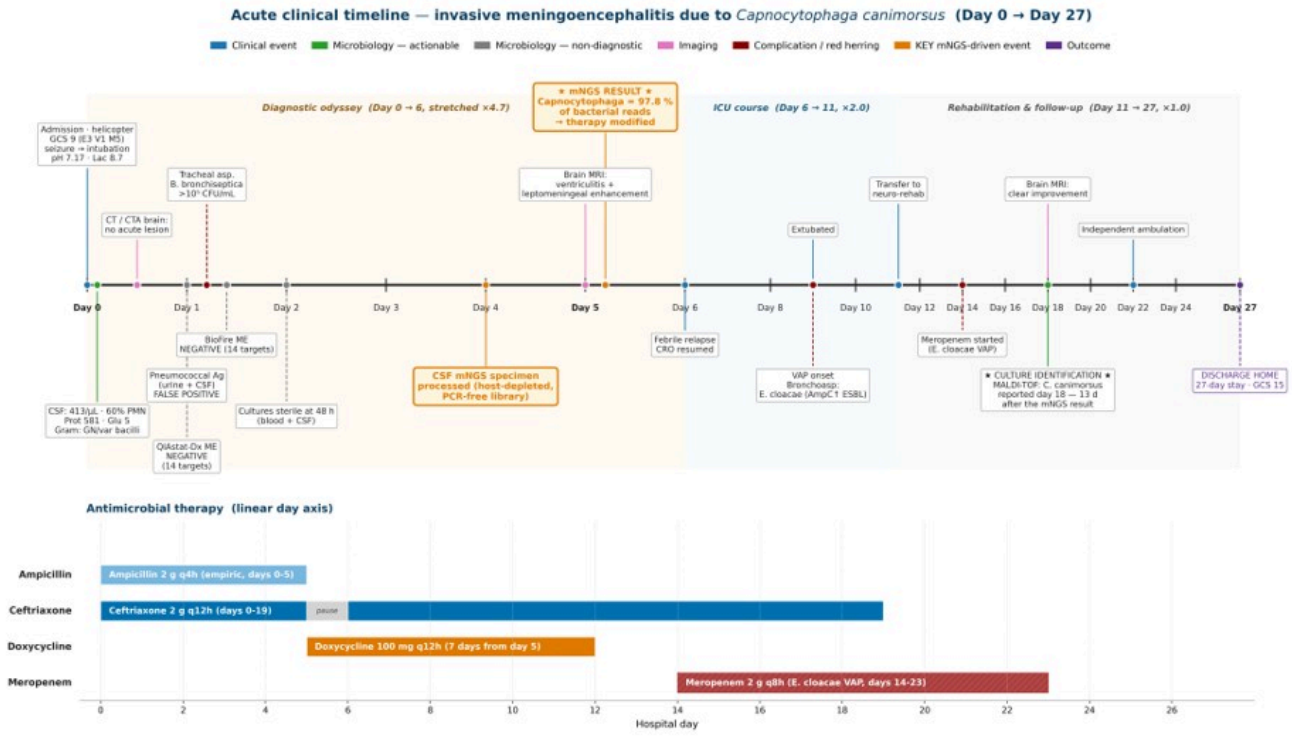


Figure 1

Acute clinical timeline (Day 0–27). Events alternate above and below the central timeline axis to avoid overlap. Each lane is colour-coded (clinical, microbiology, imaging, complication, key mNGS-driven event, outcome); the day-4 mNGS result and concurrent therapy modification are highlighted. The antimicrobial Gantt panel below shows the four parallel regimens: ampicillin (empirical, days 0–4), ceftriaxone (empirical → continued for ~19 days), doxycycline (mNGS-guided, 7 days), and meropenem (for *E. cloacae*VAP, days 9–18). Abbreviations: GCS, Glasgow Coma Scale; ME, meningoencephalitis panel; mNGS, metagenomic next-generation sequencing; RGI BWT, CARD Resistance Gene Identifier in Bowtie-2 read-mapping mode; VAP, ventilator-associated pneumonia.

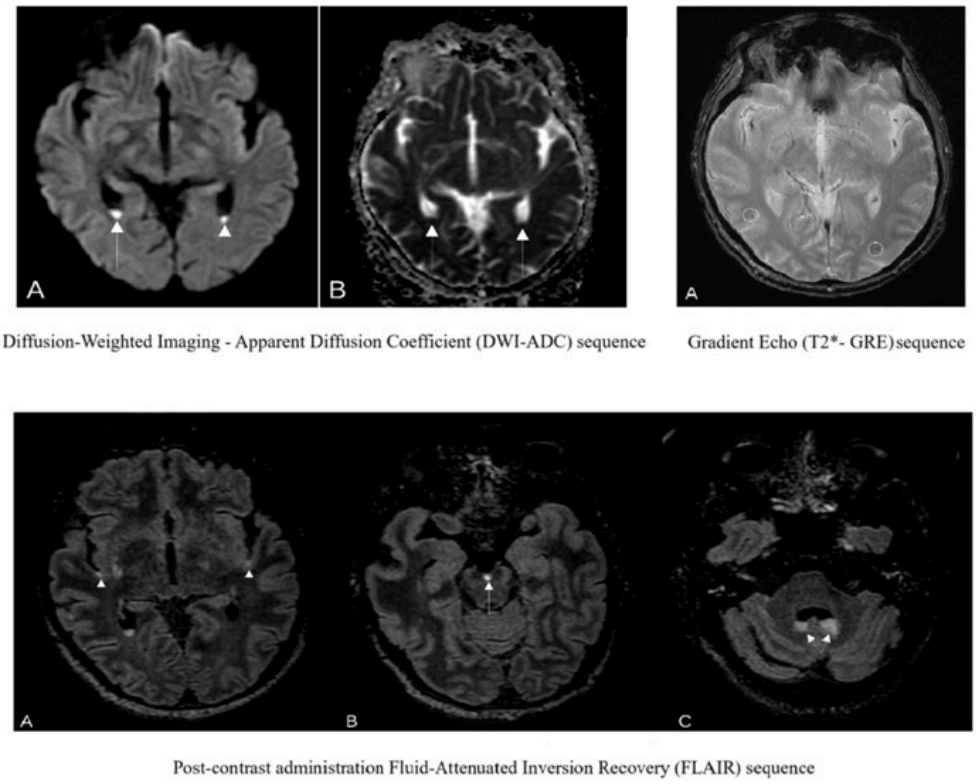


Figure 2

MRI sequences on hospital day 5.

DWI-ADC: Diffusion-weighted imaging (DWI) and corresponding apparent diffusion coefficient (ADC) map. (A) DWI shows a hyperintense (bright) signal within the occipital horns of the lateral ventricles, representing purulent debris. (B) The ADC map demonstrates corresponding hypointensity (dark signal), confirming true restricted diffusion consistent with ventriculitis.

T2*- GRE: (A) Axial T2*-weighted gradient-echo (T2* GRE) image. White circles highlight two small focal areas of signal void (blooming artifact) at the cortical-subcortical junction, consistent with cerebral microbleeds which may be directly linked to meningitis-associated infectious vasculitis.

FLAIR: Post-contrast 3D FLAIR images demonstrating focal leptomeningeal enhancement secondary to meningitis. (A) Arrow heads highlight prominent abnormal enhancement within the Sylvian fissures. (B) White arrow indicates intense inflammatory enhancement in the interpeduncular cistern. (C) Double arrow shows hyperintense debris within the fourth ventricle.

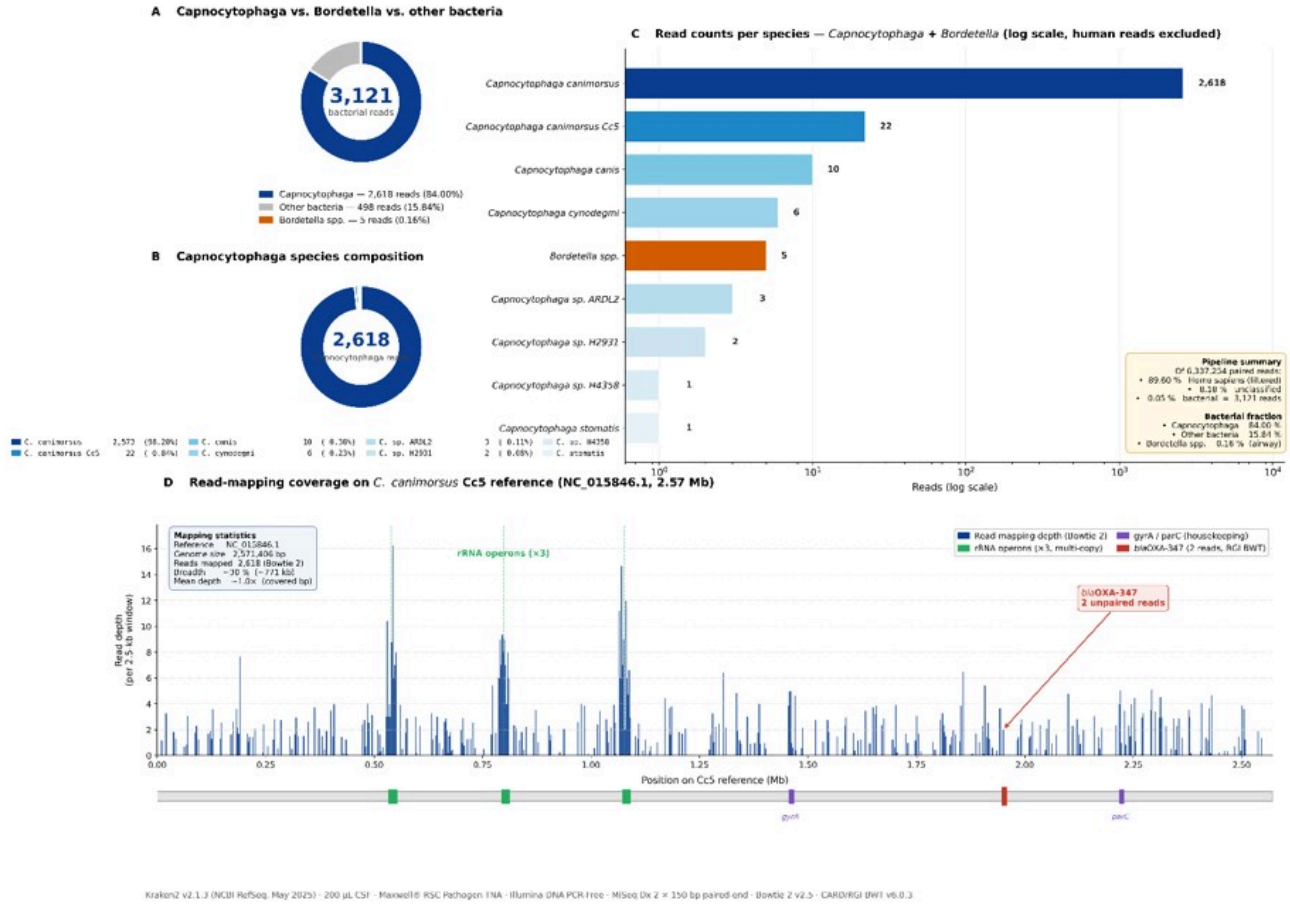


Figure 3

CSF shotgun metagenomic sequencing — taxonomic distribution. Of 6,337,254 total read pairs, 5,675,716 (89.6%) classified as *Homo sapiens*, 518,415 (8.18%) remained unclassified, and 3,121 (0.05%) classified to known bacteria. **(A)**Within the 3,121 bacterial reads, *Capnocytophaga*spp. accounted for 2,618 reads (84.0%) and *Bordetella*spp. for 5 reads (0.16%). **(B)** Within the *Capnocytophaga* genus, *C. canimorsus* accounted for 2,618 of 3,121 reads (84.0%), with trace contributions from *C. canis*, *C. cynodegmi*, *C. stomatis* and unclassified *Capnocytophaga* species. **(C)** Read counts per species on a log scale; *Homo sapiens* reads and trace eukaryotes are excluded. The *Bordetella*spp. signal is consistent with low-level airway colonisation by *B. bronchiseptica* (recovered on tracheal aspirate) rather than CNS infection.

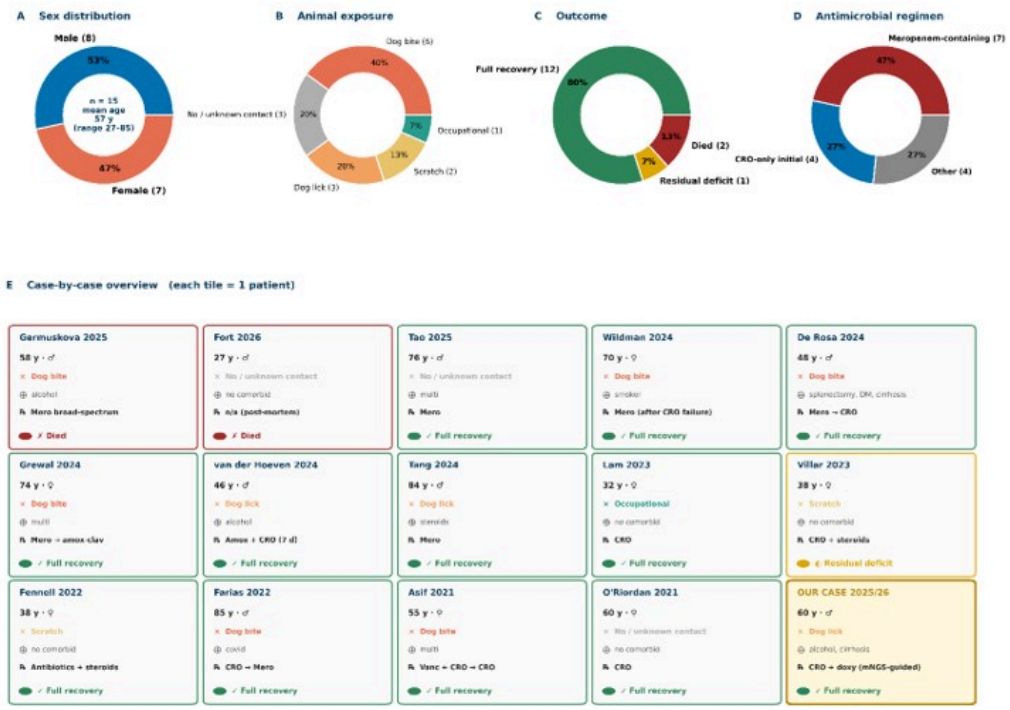


Figure 4

Recent (2021–2025) C. canimorsus* meningitis case reports — visual summary.** (A) Sex distribution. (B) Mode of animal exposure. (C) Outcome distribution. (D) Case-by-case tile grid for all 16 published cases plus the present case (gold border = index case); each tile encodes age/sex, exposure mode, comorbidities, antimicrobial regimen and outcome (tile-border colour: green = full recovery, amber = residual deficit, red = death). Overall survival: 86%; meropenem-containing regimen in 11/14 (73%); ceftriaxone-only initial regimen in 5/14. Index case: ceftriaxone + doxycycline mNGS-guided regimen.

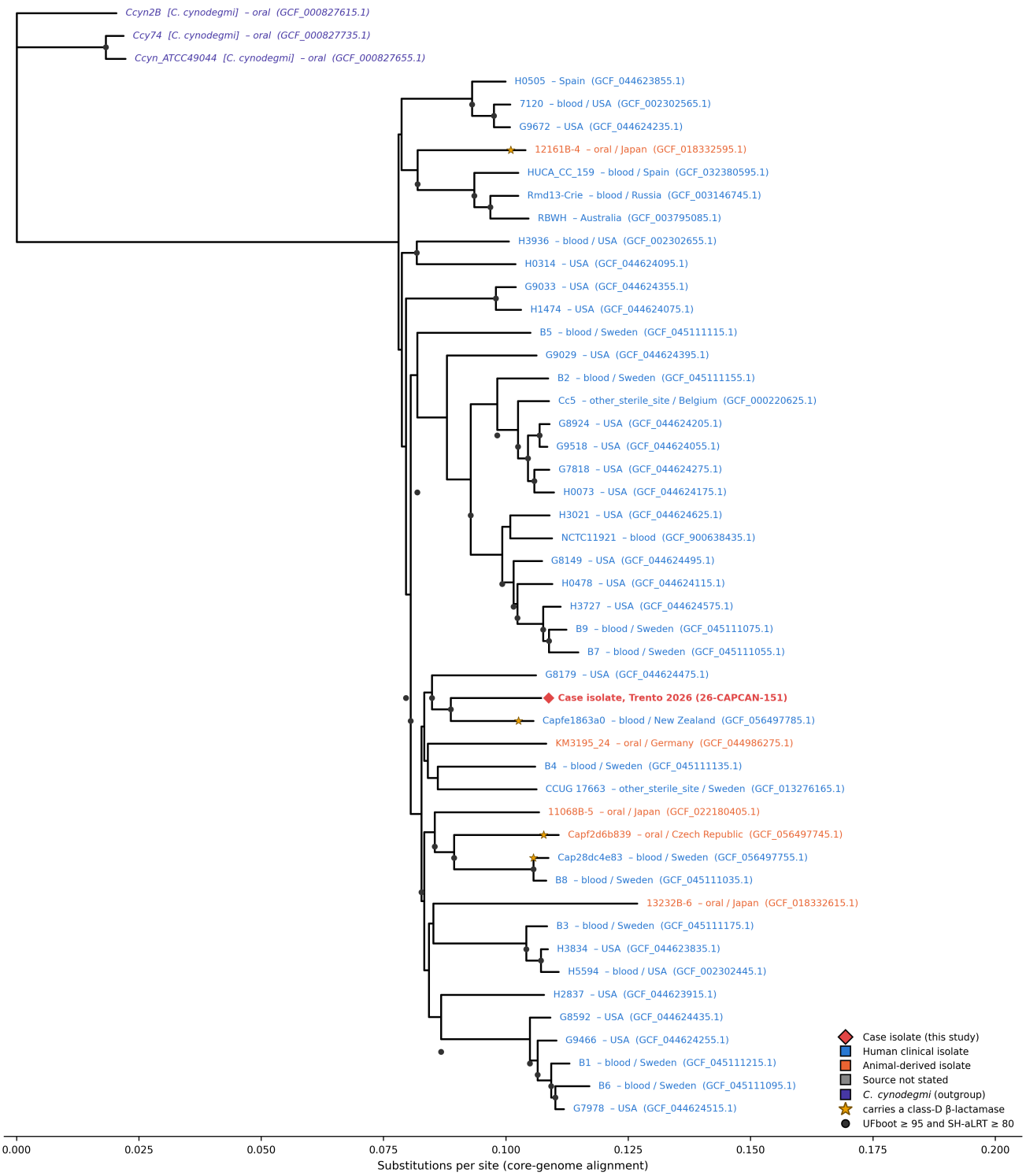


Figure 5

Core-genome maximum-likelihood phylogeny of Capnocytophaga canimorsus, comprising the case isolate, 45 public C. canimorsus genomes and three C. cynodegmi genomes used to root the tree, inferred from a 291-gene, 323,613-nucleotide alignment. Tips are coloured by isolate source; the case isolate is marked with a red diamond. Grey circles mark nodes supported by SH-aLRT >= 80% and ultrafast bootstrap >= 95%. Gold stars mark the four genomes carrying a class-D beta-lactamase; three of these come from a collection assembled by screening for beta-lactamase carriage and so do not contribute to a prevalence estimate.