Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Long-term Glucocorticoid Exposure in Angiostrongylus cantonensis Meningoencephalitis Without Eosinophilic Response—Insights Into Treatment Withdrawal From a Medical- Humanities Perspective: A case report

Zhibi Wang
Zunyi Medical University
Zhirui Xue
Zunyi Medical University
Qingyu Pu
Zunyi Medical University
Dan Zhi
Affiliated Hospital of Zunyi Medical University
Wenrui Wang
Affiliated Hospital of Zunyi Medical University
Anyong Yu
Affiliated Hospital of Zunyi Medical University
Zeling Dong
Affiliated Hospital of Zunyi Medical University
Guangli Wang
Affiliated Hospital of Zunyi Medical University
Anping Liu
724167062@qq.com
Affiliated Hospital of Zunyi Medical University

Case Report

Keywords: Angiostrongylus cantonensis, eosinophilic meningitis, glucocorticoids, metagenomic next-generation sequencing, shared decision-making

Posted Date: November 1st, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11226001/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Angiostrongylus cantonensis is the primary pathogen responsible for human eosinophilic meningitis. Atypical infection presentations lacking peripheral or cerebrospinal fluid (CSF) eosinophilia occasionally occur under immune-modulated conditions. Long-term glucocorticoid use is a plausible contributor to blunted eosinophilic inflammatory responses. This case highlights that chronic steroid-induced immune alteration may lead to diagnostically challenging, eosinophil-negative neuroangiostrongyliasis, requiring heightened clinical vigilance.

Case presentation

A 48-year-old male with a 30-year history of psoriasis and chronic irregular oral dexamethasone use presented with generalized pain, fever, and altered mental status. Admission laboratory tests revealed neither peripheral nor cerebrospinal fluid eosinophilia. CSF metagenomic next-generation sequencing (mNGS) identified 1853 specific reads of *Angiostrongylus cantonensis*, confirming the diagnosis of neuroangiostrongyliasis. Given the patient's critical neurological deterioration and family concerns regarding irreversible severe neurological sequelae, the family declined antiparasitic treatment; the standard albendazole-glucocorticoid regimen was not administered.

Conclusions

To our knowledge, this is a real-world case of molecularly confirmed *A. cantonensis* meningoencephalitis characterized by double-negative eosinophil results, strongly associated with decades-long irregular glucocorticoid exposure. Normal eosinophil counts cannot rule out parasitic neuroinfection in patients receiving chronic glucocorticoid therapy. CSF-mNGS successfully resolved this diagnostic deadlock, validating its role as a critical alternative diagnostic tool when conventional testing yields negative results. Family-initiated treatment withdrawal illustrates prevalent real-world challenges in prognostic expectation management, risk communication, and shared decision-making for severe neglected tropical central nervous system infections.

1. Introduction

Angiostrongylus cantonensis (*A. cantonensis*) is a rat-borne nematode. Humans are accidental hosts infected via ingestion of raw or undercooked mollusks, crustaceans, or vegetation contaminated with infective larvae. Following central nervous system (CNS) invasion, larvae trigger eosinophilic meningoencephalitis, the leading global cause of parasitic eosinophilic meningitis [1]. Classic clinical manifestations include headache, fever, nuchal rigidity, nausea, vomiting, and paresthesia, with peripheral and cerebrospinal fluid (CSF) eosinophilia serving as core diagnostic biomarkers [2].

Eosinophilic inflammatory responses are dynamically modulated by host immune status, infection stage, and exogenous medications. Glucocorticoids exert comprehensive inhibitory effects on eosinophil

biology: (1) enhancing CXCR4-mediated eosinophil bone marrow homing and reducing circulating eosinophil counts [3]; (2) suppressing the production of IL-3, IL-5, and GM-CSF, key cytokines sustaining eosinophil survival and activation [4]; (3) directly inducing eosinophil apoptosis and shortening cellular lifespan [5]. Notably, glucocorticoids constitute an essential component of standard therapy for neuroangiostrongyliasis, creating a clinical paradox: the very medication used for treatment may ablate the hallmark laboratory indicator required for diagnosis.

Eosinophil-negative *A. cantonensis* infection has been sporadically reported, with frequent misdiagnoses as tuberculous or viral encephalitis [6–9]. However, few published cases have described patients with decades-long irregular glucocorticoid exposure and multiple immune-metabolic comorbidities, including psoriasis, type 2 diabetes mellitus, and hypertension.Furthermore, the full sequential clinical decision trajectory—initial refusal of high-cost molecular testing, consent after repeated clinical counselling, and subsequent withdrawal of antiparasitic therapy upon definitive diagnosis—has rarely been documented within a single case report. We report a case of *A. cantonensis* meningoencephalitis occurring in a patient receiving chronic, irregular dexamethasone. The patient exhibited absence of eosinophilia in both peripheral blood and CSF, and the diagnosis was definitively confirmed by CSF metagenomic next-generation sequencing (mNGS). We (1) elaborate the mechanistic basis of glucocorticoid-mediated eosinophil suppression; (2) highlight the clinical caveat that normal eosinophil counts cannot rule out A. cantonensis infection in immunocompromised patients with chronic steroid exposure; (3) discuss real-world barriers to shared decision-making and humanistic considerations in clinical practice arising from this unique family decision-making process.

2. Case Report

A 48-year-old male presented to the emergency department with a 10-day history of generalized body pain, 3 days of persistent fever, and 1 day of progressive altered consciousness. The patient had resided and worked in Guangzhou with a habitual history of drinking unboiled water. Symptom onset occurred before he returned to his hometown in Wuchuan County, Guizhou Province. He received preliminary evaluations at local and municipal tertiary hospitals without definitive diagnosis and was subsequently transferred to our emergency department for further management.

His past medical history was significant for long-standing psoriasis, type 2 diabetes mellitus, and newly diagnosed hypertension. Psoriasis had persisted for over 30 years, managed with irregular long-term oral dexamethasone (5 mg) and chlorpheniramine maleate (10 mg). Type 2 diabetes mellitus was diagnosed five years prior, treated with irregular subcutaneous insulin aspart and oral extended-release metformin, without regular blood glucose monitoring. Hypertension was diagnosed 10 days before admission and controlled with extended-release felodipine (5 mg once daily).

2.1 Physical Examination

On admission, the patient presented with fever (37.2°C), tachycardia (112 bpm), tachypnea (32 breaths/min), and hypertension (143/102 mmHg). The oxygen saturation was 97% under nasal cannula oxygen supplementation with a FiO_2 of 40%. Neurological examination demonstrated a Glasgow Coma Scale score of 9 (E2V2M5); the patient remained comatose but responsive to painful stimuli. Bilateral pupils were equal and round (approximately 3 mm) with brisk light reflexes. Generalized scaly cutaneous lesions were observed, while superficial lymphadenopathy was absent. Nuchal rigidity and jugular venous distension were noted. Pulmonary auscultation revealed symmetric breath sounds with scattered crackles. Cardiac rhythm was regular at 112 bpm. The abdomen was soft and non-tender, and no lower extremity edema was detected. Motor function could not be adequately assessed due to impaired consciousness.

2.2 Auxiliary Examinations

External hospital tests showed elevated inflammatory markers (ESR, CRP) and glycemic levels. Urinalysis revealed positive ketones, hematuria, and glycosuria. Peripheral blood eosinophil counts remained normal. Other hematological parameters are summarized in Table 1. CSF analysis demonstrated pleocytosis without eosinophils (Table 2). Cranial and thoracic imaging showed no intracranial lesions but bilateral pulmonary inflammatory changes with partial atelectasis.

During hospitalization, arterial blood gas analysis indicated metabolic acidosis with respiratory compensation. Laboratory tests revealed elevated inflammatory and coagulation indices, monocytosis without eosinophilia, and persistent positive urinary glucose, leukocytes, blood, protein, and ketones. Autoantibody screening, procalcitonin, and fungal cultures were negative. Admission lumbar puncture confirmed mononuclear-predominant CSF pleocytosis without eosinophilia (Table 2). Chest CT identified bilateral lower-lobe pneumonia with small pleural effusions, while cranial CT showed no structural abnormalities.

Table 1
Complete blood count (CBC) parameters prior to admission and during hospitalization

Parameter	Outside hospital findings	During hospitalization
WBC(×10⁹/L)	5.47	5.93
NEUT(×10⁹/L)	3.28	4.27
LYMPH(×10⁹/L)	1.15	0.71
EOS(×10⁹/L)	0.38	0.42
BASO(×10⁹/L)	0	0
Hb (g/L)	114	91
PLT(×10⁹/L)	243	207

Table 2
Cerebrospinal fluid (CSF) parameters prior to admission and during hospitalization

Parameter	Outside hospital findings	During hospitalization
ICP (cmH2O)	250	260
Appearance	Colorless and transparent	Colorless and transparent
Pandy's test	+	+
TNCC(10^6/L)	530	120
WBC(10^6/L)	524	100
EOS (%)	-	-
LDH(U/L)	29	42
TP (mg/L)	1202	1247
ADA(U/L)	0.67	0.80

2.3 Diagnostic and Treatment Course

Admission (Day 2)

The patient was admitted with a provisional diagnosis of unexplained CNS infection. Despite negative peripheral and CSF eosinophilia, *A. cantonensis* infection was included in the differential diagnosis given his history of raw water ingestion. Repeat lumbar puncture and CSF-mNGS were immediately recommended for etiological confirmation. However, the family declined repeated lumbar puncture and refused mNGS due to its high out-of-pocket cost. Empirical anti-infective therapy, intracranial pressure reduction, and supportive life-sustaining care were initiated accordingly.

Disease progression (Days 3–6)

The patient’s clinical status deteriorated progressively with worsening consciousness disturbance. On Day 6, the clinical team conducted intensive family counselling, emphasizing that conventional laboratory tests failed to identify the causative pathogen and that only unbiased mNGS could achieve comprehensive pathogen detection. Without definitive etiological diagnosis, targeted therapy was unfeasible, and the prognosis was extremely poor. After repeated persuasion, the family consented to repeated lumbar puncture and CSF-mNGS testing.

Definitive diagnosis and treatment withdrawal (Days 7–8)

On Day 7, CSF-mNGS yielded positive results, identifying 1853 specific reads of *A. cantonensis* with a relative abundance of 52.27%, confirming *A. cantonensis* meningoencephalitis (Fig. 1). The standard albendazole combined with glucocorticoid regimen was formulated, and the diagnostic basis, treatment

protocol, expected efficacy, and potential adverse reactions were fully communicated to the family. Nevertheless, the family remained highly concerned about the patient's critical neurological impairment, fearing persistent unconsciousness and irreversible severe CNS sequelae despite aggressive intervention. After careful consideration, the family decided to withdraw antiparasitic treatment. The patient was discharged against medical advice on Day 8 without receiving pathogen-targeted therapy. The timeline of the patient's clinical manifestations, diagnoses and treatments is shown in Fig. 2.

3. Discussion

Typical *A. cantonensis* CNS infection manifests as eosinophilic meningitis, in which CSF eosinophilia (> 10% or absolute count > 10×10^6/L) serves as a core diagnostic indicator [2]. In contrast, our patient presented with a double-negative eosinophil phenotype in both peripheral blood and CSF, representing an atypical presentation associated with substantial risks of missed or delayed diagnosis.

3.1 Potential mechanisms underlying glucocorticoid-mediated eosinophil suppression

Thirty years of prolonged, irregular glucocorticoid exposure is the most plausible cause of absent eosinophilic responses in this patient. Serial tests from external and our institutional laboratories consistently confirmed persistent eosinopenia.

Glucocorticoids exert multi-modal inhibitory effects on eosinophil trafficking and survival. First, they facilitate CXCR4-dependent eosinophil bone marrow homing, rapidly reducing circulating eosinophil counts [3]. Second, they downregulate eosinophil-supporting cytokines, including IL-3, IL-5, and GM-CSF [4]. IL-5 is indispensable for eosinophil differentiation and survival; its suppression directly diminishes peripheral and tissue eosinophil abundance. Third, glucocorticoids trigger eosinophil apoptosis and shorten cellular lifespan [5]. Preclinical studies further demonstrate that dexamethasone downregulates meningeal and CSF MMP-9 expression, oxidative stress pathways, and 14-3-3 protein levels, thereby attenuating blood–brain barrier damage and reducing eosinophil recruitment in experimental angiostrongyliasis [10, 11]. Collectively, these mechanisms constitute a robust suppressive cascade. Additionally, early larval invasion prior to robust Th2 immune activation and host genetic variation may further modulate individual eosinophilic responses [12].

3.2 Clinical warning: normal eosinophil counts cannot exclude *A. cantonensis* infection

This diagnostic caveat has been documented in clinical guidelines and previous case series. Centers for Disease Control and Prevention (CDC) guidelines indicate that CSF eosinophilia > 10% strongly supports angiostrongyliasis, whereas normal eosinophil levels cannot rule out infection [13]. Eosinophil-negative cases have been frequently misdiagnosed as tuberculous meningitis [7]. The novelty of the present case lies in its real-world illustration of atypical eosinophil-negative neuroangiostrongyliasis in a patient with

combined immune-metabolic comorbidities and long-term exogenous steroid exposure. Clinicians should maintain high suspicion for *A. cantonensis* infection in patients with compatible epidemiological exposure, even with normal eosinophil results. Although our team retained *A. cantonensis* in the differential diagnosis throughout hospitalization, family refusal of unreimbursed, high-cost mNGS delayed definitive diagnosis by six days. This real-world barrier highlights the necessity of balanced counselling regarding the advantages and limitations of advanced molecular diagnostics.

3.3 Diagnostic performance of mNGS in atypical neuroangiostrongyliasis

In the absence of classic eosinophilic biomarkers, high-abundance CSF-mNGS successfully established the definitive etiological diagnosis. Previous studies have validated mNGS efficacy for neuroangiostrongyliasis, with mNGS positivity often preceding serological seroconversion [8, 14]. In this diagnostic deadlock characterized by absent classic markers and initial family refusal of testing, CSF-mNGS played a decisive diagnostic role, confirming its value as an alternative diagnostic modality when conventional workups are non-diagnostic. Nevertheless, out-of-pocket costs remain a major clinical limitation, necessitating individualized mNGS indication selection based on clinical scenarios.

3.4 Medical humanities reflection on treatment withdrawal: surrogate decision-making and shared decision-making

Despite definitive pathogen identification, the patient's surrogates declined standard antiparasitic therapy, and the patient was discharged against medical advice without albendazole-glucocorticoid intervention. This unfavorable outcome persisted despite repeated clinical communication. This case presents a unique three-stage family decision trajectory: initial refusal of mNGS testing, conditional consent after counselling, and post-diagnosis treatment withdrawal, offering insights into prognostic expectation management and shared decision-making in critical infectious diseases.

First, severe infectious CNS diseases impose substantial challenges for therapeutic expectation management. The albendazole-glucocorticoid combination is a well-established effective regimen for neuroangiostrongyliasis [15]. However, our patient presented with severe coma, placing enormous psychological pressure on family surrogates. Information asymmetry and initial distrust toward high-cost molecular testing amplified prognostic uncertainty. Time constraints in acute critical care further hinder high-quality risk communication.

Second, shared decision-making is difficult to implement in emergent critical settings. Shared decision-making emphasizes collaborative dialogue between clinicians and surrogates, integrating clinical evidence with patient values and preferences [16, 17]. In this case, the patient lacked decision-making capacity, and family surrogates bore heavy cognitive and emotional burdens. Treatment refusal stemmed from multifaceted concerns, including pessimistic prognostic expectations, fear of permanent neurological sequelae, and economic barriers reflected in the initial mNGS refusal. Treatment withdrawal represented a comprehensive real-world trade-off rather than arbitrary medical refusal.

Third, structural social and medical factors contributed to final decision-making. Long-term irregular self-medication and fragmented healthcare-seeking behavior imply limited health literacy and unequal healthcare accessibility, which adversely affected crisis-period decision-making. Self-funded mNGS created a direct economic barrier leading to diagnostic delay. Treatment withdrawal cannot be simply attributed to “family choice”; it results from the interaction of individual preference, medical accessibility, insurance coverage, and clinician–patient trust [18].

This case yields three clinical implications for severe complex CNS infections: (1) establish realistic therapeutic expectations at early disease stages and objectively communicate treatment prospects and sequela risks after diagnosis confirmation; (2) proactively identify financial, cognitive, and emotional decision barriers and deliver targeted support; (3) integrate shared decision-making throughout the entire clinical course rather than only at late-stage decision points.

4. Conclusions

We report a unique case of *A. cantonensis* meningoencephalitis in a patient with long-term irregular glucocorticoid exposure and multiple immune-metabolic comorbidities, presenting with double-negative eosinophil results in peripheral blood and CSF. Chronic glucocorticoid-mediated immune suppression is the most likely cause of this atypical diagnostic phenotype. Normal eosinophil counts cannot exclude *A. cantonensis* infection in patients with steroid-induced immune modulation. CSF-mNGS effectively resolved this diagnostic dilemma and serves as a powerful alternative diagnostic tool for conventional test-negative parasitic CNS infections. The sequential family decision pathway (test refusal→counselling-mediated consent →post-diagnosis treatment withdrawal) reflects prevalent real-world challenges involving diagnostic affordability, prognostic expectation framing, and shared decision-making. Optimal management of neglected tropical CNS infections requires integrated strategies combining precise molecular diagnosis, standardized treatment, and humanistic care, while fully acknowledging real-world socioeconomic barriers limiting advanced diagnostic access.

Abbreviations

CSF Cerebrospinal fluid

mNGS Metagenomic next-generation sequencing

CNS Central nervous system

CXCR4 C-X-C motif chemokine receptor 4

IL-3 Interleukin-3

IL-5 Interleukin-5

GM-CSF Granulocyte-Macrophage Colony-Stimulating Factor

Cantonensis Angiostrongylus cantonensis
ESR *E*rythrocyte sedimentation rat

CRP C-reactive protein

CBC Complete blood count

WBC White blood cell

NEUT Neutrophil cell

LYMPH Lymphocyte cell

EC Eosinophil cell

BASO Basophil cell

HB Hemoglobin

PLT Platelet

LDH Lactate dehydrogenase

ADA Adenosine deaminase

TP Total protein

ICP Intracranial pressure

TNCC total nucleated cell count

MMP-9 matrix metalloproteinase-9

CDC Centers for Disease Control and Prevention

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Affiliated Hospital of Zunyi Medical University(approval number: KLL-2026-284). This study complied with relevant guidelines and regulations.

Consent for publication

Written informed consent was obtained from the patient’s surrogate for the publication of this case report and any accompanying data and images.

Availability of data and materials

The clinical records of the patient are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests

Author Contributions

ZBW: Writing original draft. ZRX: Data analysis. QYP: Clinical data collection. DZ: Resources. WRW: Investigation. AYY: Conceptualization. ZLD, GLW: Laboratory data curation. APL: Data analysis, writing review and editing. All authors read and approved the final manuscript.

Funding Sources

This work was supported by the Guizhou Province Clinical Research Center for Emergency Medicine (No. LCZX [2025]004), the High-level Innovative Talents of Guizhou Province (GCC [2023]081), the Zunyi Science and Technology Project (No. Zunshi kehe HZ [2024]182), and the University-level Graduate Education Innovation Program of Zunyi Medical University (YJSJG2025019).

Acknowledgments

We thank the patient and his family for their participation in this study.

References

1. Wang QP, Lai DH, Zhu XQ, et al. Human angiostrongyliasis. Lancet Infect Dis. 2008;8(10):621–30.
2. Slom TJ, Cortese MM, Gerber SI, et al. An outbreak of eosinophilic meningitis caused by *A. cantonensis* in travelers returning from the Caribbean. N Engl J Med. 2002;346(9):668–75.
3. Farahi N, Paiva R, Loutsios C, et al. Glucocorticoid-induced eosinopenia results from CXCR4-dependent bone marrow migration. Blood. 2020;136(19):2167–78.
4. Gaspar Elsas MI, Vargaftig BB, Xavier Elsas P. Do glucocorticoids enhance eosinopoiesis? Trends Pharmacol Sci. 2000;21(11):417–20.
5. Vieira BM, Paiva MB, Gaspar-Elsas MIC, et al. Coordinated regulation of eosinophil production and migration by glucocorticoids, prostaglandins, and cysteinyl-leukotrienes. Int Immunopharmacol. 2025;148:114067.
6. Amornpojnimman T, Sanghan N, Ekpitakdamrong N, et al. Angiostrongylosis meningomyelitis without blood eosinophilia. J Infect Dev Ctries. 2021;15(12):1933–6.
7. Lin MG, Wang AS, Wang W, et al. Angiostrongyliasis cantonensis misdiagnosed as tuberculous meningitis: two case reports and literature review. J Clin Pulm Med. 2009;14(8):1047–8.

8. Li H, Chen Y, Wu X, et al. Central nervous system infection by *A. cantonensis* in children: experience from Guangdong, China. BMC Infect Dis. 2025;25:1560.
9. Luo XJ, Cao K, Zhang Y, et al. Clinical features of*A. cantonensis* meningitis in children and diagnostic value of metagenomic next-generation sequencing. Chin J Lab Med. 2026;49(3):215–21.
10. Tsai HC, Chen YS, Hsu SM, et al. Dexamethasone downregulates the expressions of MMP-9 and oxidative stress in mice with eosinophilic meningitis caused by *A. cantonensis* infection. Parasitology. 2021;148(2):187–97.
11. Tsai HC, Chung LY, Chen ER, et al. Dexamethasone downregulated the expression of CSF 14-3-3β protein in mice with eosinophilic meningitis caused by *A. cantonensis* infection. Am J Trop Med Hyg. 2013;89(6):1089–93.
12. Zhou H, Lu Y, Wei H, et al. Stat3/IL-6 signaling mediates sustained pneumonia induced by *A. cantonensis*. PLoS Negl Trop Dis. 2022;16(5):e0010461.
13. Centers for Disease Control and Prevention. Clinical Testing and Diagnosis for Rat Lungworm (*A. cantonensis*). 2024.
14. Zhao JH, Wang Y, Zhang L, et al. Treatment of a rare and severe infection of central nervous system by *A. cantonensis*: a case report. World J Radiol. 2025;17(2):102108.
15. Jacob J, Steel A, Lin Z, et al. Clinical efficacy and safety of albendazole and other benzimidazole anthelmintics for rat lungworm disease (neuroangiostrongyliasis): a systematic analysis of clinical reports and animal studies. Clin Infect Dis. 2022;74(7):1293–302.
16. Elwyn G, Frosch D, Thomson R, et al. Shared decision making: a model for clinical practice. J Gen Intern Med. 2012;27(10):1361–7.
17. King JS, Eckman MH, Moulton BW. The potential of shared decision making to reduce health disparities. J Law Med Ethics. 2011;39(Suppl 1):30–3.
18. Marmot M, Allen J, Bell R, et al. WHO European review of social determinants of health and the health divide. Lancet. 2012;380(9846):1011–29.

Figures

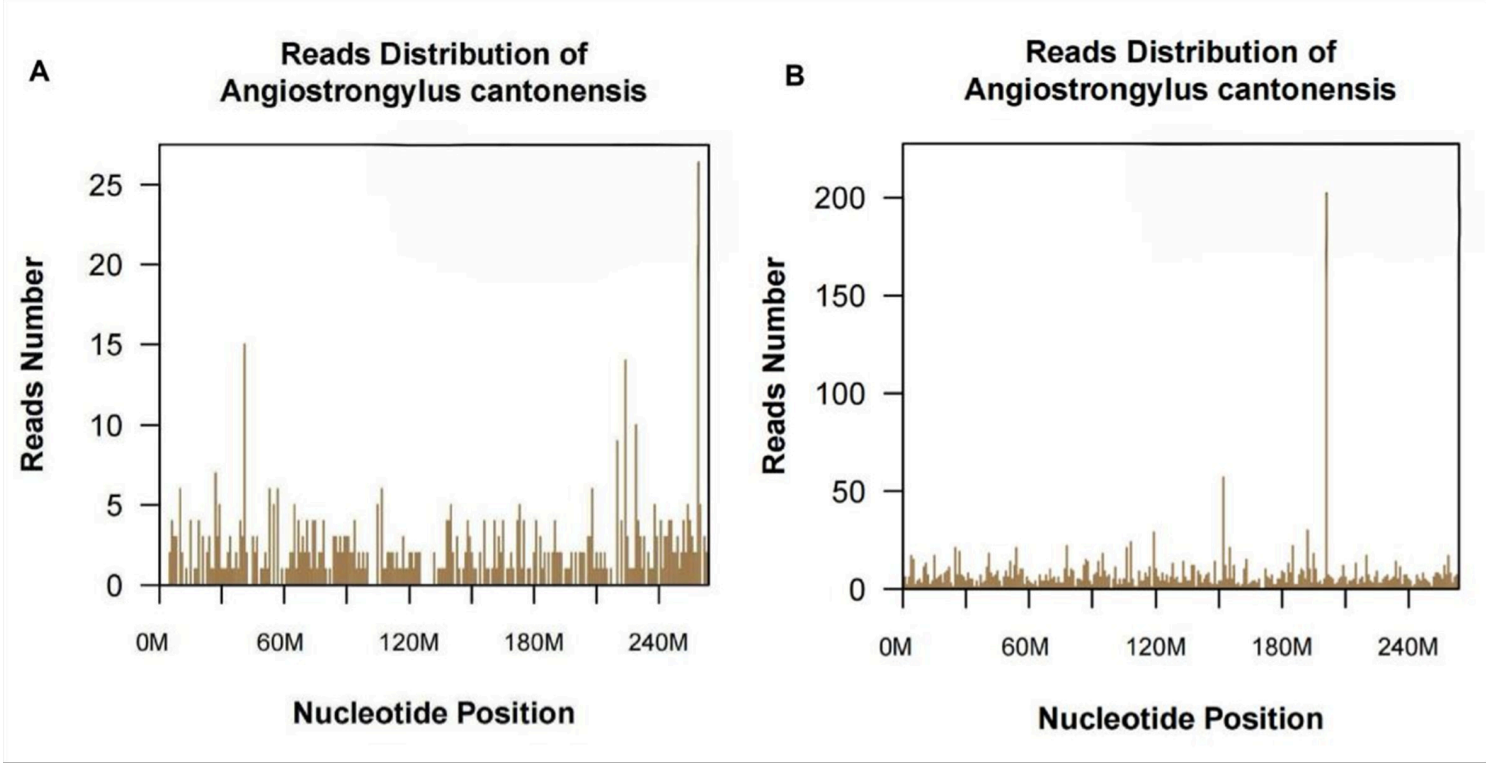


Figure 1

Genomic read distribution of Angiostrongylus cantonensis detected by DNA-seq and RNA-seq using the same cerebrospinal fluid specimen. (A) DNA sequencing; (B) RNA sequencing.

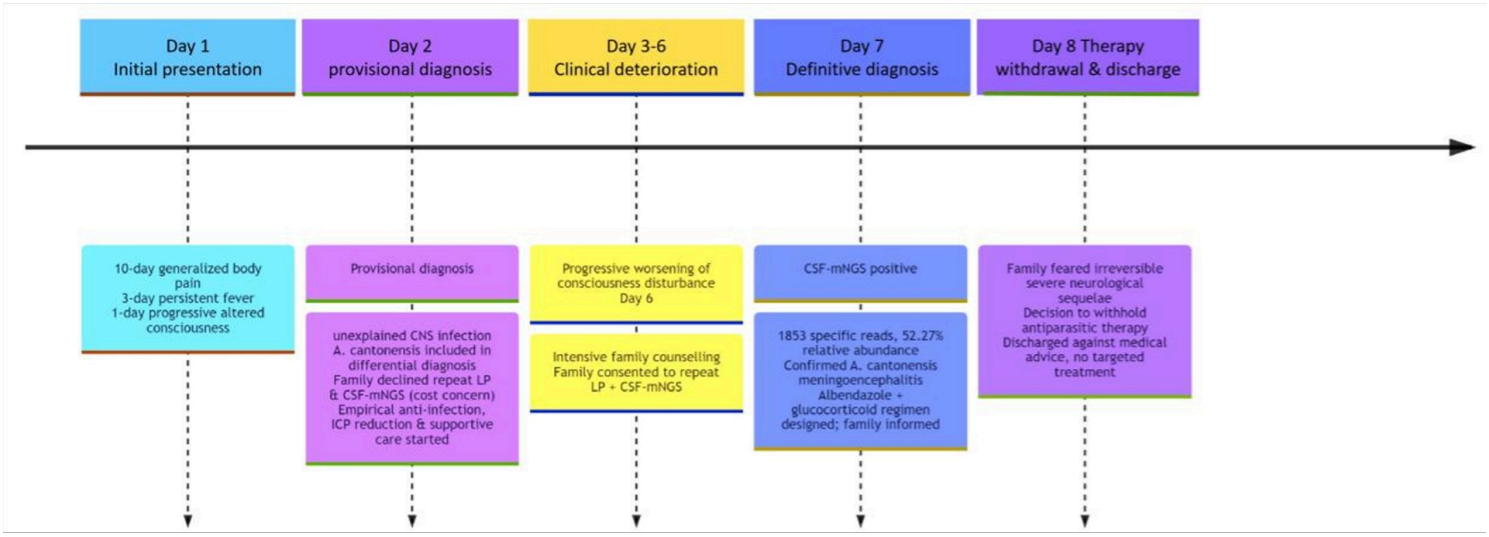


Figure 2

Clinical timeline of a 48-year-old male with Angiostrongylus cantonensis meningoencephalitis showing clinical presentation, diagnostic workup, and final therapeutic withdrawal and discharge against medical advice.