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Fatal Tuberculous Meningitis With Extensive Demyelinating Encephalomyelitis Consistent With Acute Disseminated Encephalomyelitis in an Adult With Concurrent Mixed Malaria: A Case Report

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Case Report

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Abstract

Background

Tuberculous meningitis (TBM) can cause severe neurological injury, while acute disseminated encephalomyelitis (ADEM) may produce multifocal brain and spinal cord lesions. Distinguishing infection from an overlapping inflammatory demyelinating process can be challenging.

Case presentation

A 45-year-old Ethiopian man from a malaria-endemic area developed two weeks of feverishness, headache, chills, myalgia, and arthralgia, followed by behavioral change, vomiting, seizure-like episodes, urinary retention, progressive limb weakness, and declining consciousness. Mixed Plasmodium falciparum and P. vivax infection had been documented before referral. Brain MRI showed multiple asymmetric, poorly marginated T2/FLAIR-hyperintense cerebral lesions; spinal MRI demonstrated longitudinally extensive thoracic cord abnormalities extending to the conus. Cerebrospinal fluid (CSF) opening pressure was 260 mm H_2O, white-cell count 280/μL with 84% lymphocytes, protein 320 mg/dL, and CSF-to-serum glucose ratio 0.22. CSF GeneXpert MTB/RIF detected Mycobacterium tuberculosis complex, with no rifampicin resistance detected. Malaria parasitemia declined during treatment, and subsequent smears were negative. Despite antituberculous, antimalarial, antibacterial, antiviral, corticosteroid, and supportive treatment, the patient developed profound hyponatremia, refractory hypokalemia, suspected aspiration pneumonia, respiratory failure, cardiac arrest, and refractory septic shock. He died during the fifth day of intensive care.

Conclusion

This case describes molecularly confirmed TBM with extensive cerebral and spinal cord lesions radiologically suggestive of ADEM or an ADEM-like process in a patient with concurrent mixed malaria. It highlights the need to investigate infectious and inflammatory causes in parallel, monitor electrolytes closely, and recognize the potential for rapid deterioration.

Introduction

Tuberculous meningitis (TBM) is a severe form of extrapulmonary tuberculosis associated with substantial mortality and neurological disability. Its presentation may be subacute, with headache, fever, altered mental status, cranial or long-tract deficits, seizures, and progressive impairment of consciousness. Cerebrospinal fluid typically shows lymphocytic pleocytosis, elevated protein, and reduced glucose, although findings vary and microbiological confirmation may be difficult [3–6].

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating syndrome characterized by encephalopathy and multifocal neurological deficits, usually with large, poorly marginated T2/FLAIR-hyperintense lesions on MRI. In adults, ADEM can resemble infectious encephalitis, vasculitis, other antibody-associated demyelinating disorders, and vascular or metabolic disease [1, 2]. CNS infection and an ADEM-like inflammatory process may be difficult to distinguish clinically; therefore, imaging must be interpreted alongside CSF and microbiological findings.

We report a fatal case of molecularly confirmed TBM with extensive cerebral and spinal cord lesions interpreted radiologically as highly characteristic of ADEM, in a patient with documented mixed malaria infection. The case highlights the complexity of diagnosing overlapping infectious and inflammatory CNS disease and the importance of cautious interpretation when a complete diagnostic work-up is not available.

Case presentation

Patient information and initial presentation

A 45-year-old Ethiopian male farmer from Chilga Woreda, Kenweta Kebele, with no documented history of diabetes, hypertension, chronic kidney disease, or chronic liver disease, was admitted on 15/10/2018 E.C. (Ethiopian calendar; the corresponding Gregorian date should be confirmed from the original hospital record). He had been relatively well until approximately two weeks before presentation, when he developed intermittent generalized headache, feverishness, chills, rigors, myalgia, and arthralgia. He lived in a malaria-endemic area and had a history of repeated malaria episodes.

At a health center, rapid diagnostic testing and peripheral blood film reportedly supported mixed P. falciparum and P. vivax malaria. He received a three-day course of artemether–lumefantrine (Coartem), but symptoms did not improve; vomiting may have impaired oral drug intake or absorption. At Aykel Primary Hospital, cerebral malaria was considered and intravenous artesunate was administered (the supplied presentation records four doses over approximately 48 hours). His mental status subsequently deteriorated.

Approximately five days before referral, he developed bizarre behavior, two episodes of non-projectile vomiting, urinary retention, confusion, and recurrent abnormal movements involving flexion and extension of the limbs, upward rolling of the eyes, and drooling of saliva, reported at approximately three episodes per day. Weakness progressed from the left lower limb to the right lower limb and then the right upper limb over several days. He became comatose and was referred for evaluation of possible cerebral malaria, pyogenic meningitis, and an intracranial space-occupying lesion.

Examination on admission

At emergency department assessment, he was stuporous and confused, with a Glasgow Coma Scale (GCS) score of 10/15 (E3V2M5). Recorded vital signs were blood pressure 149/112 mmHg, pulse 102 beats/minute, respiratory rate 24 breaths/minute, temperature 37.9°C, oxygen saturation 91% on room air, and random blood glucose 150 mg/dL. Pupils were initially mid-sized and reactive, with no facial deviation documented. Sensory impairment was reported up to the umbilical level. Tone was initially recorded as normal, and deep tendon reflexes were 2+. A nasogastric tube was in place.

Subsequent neurological examinations documented right facial deviation, anisocoria and later impaired or absent pupillary reactivity, hypotonia of the lower limbs, right upper-limb power of 3/5, and bilateral lower-limb power of 0/5. Pain sensation was impaired to the umbilical level. Meningeal signs were recorded as negative. These evolving findings were consistent with severe multifocal CNS involvement and a spinal cord syndrome.

Laboratory and malaria investigations

Initial complete blood count showed a white blood cell count of 3,100/µL with 87.9% neutrophils and 7.8% lymphocytes, hemoglobin 15.7 g/dL, hematocrit 37.4%, and platelet count 39,000/µL. Initial serum sodium was 126.36 mmol/L, potassium 3.43 mmol/L, chloride 96.62 mmol/L, and calcium 0.97 mmol/L.

The supplementary laboratory record reported a positive malaria rapid diagnostic test for pan-malarial antigen and P. falciparum-specific antigen. The pre-referral blood film reportedly demonstrated mixed P. falciparum and P. vivax infection, with parasitemia estimated at 3.8% (approximately 170,000 parasites/µL). At emergency department assessment, rare P. falciparum ring forms were reported, with no P. vivax asexual forms and parasitemia estimated at 0.3% (approximately 12,000 parasites/µL). Repeat smears dated 17/10/2018 E.C. and 19/10/2018 E.C. were reported negative for malaria parasites, while the platelet count rose to 102,000/µL and then 116,000/µL. These findings document a marked decline in detectable parasitemia during antimalarial treatment; the exact cumulative duration of artesunate across pre-referral and in-hospital care was not fully documented.

Serial laboratory results showed worsening hyponatremia, with sodium declining to 113.3 mmol/L and then 111.9 mmol/L. Sodium later rose to 120.7 mmol/L and 134 mmol/L following salt replacement documented in the clinical notes. Potassium declined from 3.43 mmol/L to 3.03, 3.09, 2.9, and finally 2.13 mmol/L despite supplementation, including intravenous replacement in the ICU. Other reported results included ESR 58 mm/hour, non-reactive ANA, vitamin B12 654, creatinine 0.57 and then 0.46 mg/dL, BUN 19 mg/dL, AST 26 U/L, ALT 17–20 U/L, and albumin approximately 3.0–3.13 g/dL. SIADH was considered in the clinical notes, but serum osmolality, urine osmolality, urine sodium, thyroid function, and adrenal evaluation results were not supplied; therefore, SIADH cannot be considered confirmed.

Neuroimaging

Initial head CT demonstrated hypodensity involving the left anterior temporal cortex and subcortical white matter and the left cerebral peduncle, without post-contrast enhancement or significant midline shift. A punctate CSF-density hypodensity was described in the left thalamus, without enhancement.

Brain MRI with and without gadolinium showed multiple bilateral, asymmetric, large, poorly marginated areas of increased T2/FLAIR signal in the subcortical and deep central white matter of both cerebral hemispheres. A prominent non-enhancing T2/FLAIR-hyperintense lesion involved the left anterior temporal cortex and adjacent subcortical white matter, extending inferiorly into the left cerebral peduncle. The large white matter lesions showed faint, patchy peripheral restricted diffusion. Minimal patchy, non-confluent open-ring or punctate enhancement was described along the margins of some lesions. There was no significant mass effect or midline shift. Faint patchy leptomeningeal enhancement was present along the basal cisterns. The radiology impression considered the distribution highly characteristic of ADEM, while retaining complicated meningoencephalitis, including tuberculous meningitis with secondary vasculitis or infarction, as an important differential diagnosis.

Spinal MRI showed an extensive, contiguous, poorly marginated T2-hyperintense lesion extending from the mid-thoracic spinal cord to the conus medullaris, spanning more than three vertebral segments. Cord edema was most pronounced from T8 to T10, corresponding to the documented sensory level at the umbilicus. Mild diffuse lower thoracic cord swelling and diffuse patchy central and leptomeningeal enhancement were reported. The imaging impression was longitudinally extensive transverse myelitis.

Cerebrospinal fluid findings

The CSF report is dated 17/10/2018 E.C., as confirmed by the authors. The opening pressure was elevated at 260 mm H_2O. CSF was slightly turbid with faint xanthochromia, and a fine web-like clot or pellicle was reported after 24 hours. CSF protein was markedly elevated at 320 mg/dL, glucose was 34 mg/dL with simultaneous serum glucose 150 mg/dL, and the CSF-to-serum glucose ratio was 0.22.

CSF white blood cell count was 280 cells/μL, with 84% lymphocytes, 12% neutrophils, and 4% monocytes/histiocytes. The red blood cell count was 12 cells/μL. Gram stain showed no bacteria, and bacterial culture had no growth to date while the patient was receiving ceftriaxone and vancomycin. AFB smear was negative. CSF GeneXpert MTB/RIF detected Mycobacterium tuberculosis complex, with rifampicin resistance not detected. CSF adenosine deaminase was 14.2 U/L. Cryptococcal antigen and India ink preparation were negative, as were the reported HSV-1, HSV-2, and VZV PCR tests.

The CSF profile—raised opening pressure, lymphocytic pleocytosis, markedly elevated protein, low glucose ratio, and positive CSF GeneXpert—supports a diagnosis of tuberculous meningitis (TBM) [3–6]. A negative AFB smear does not negate the positive molecular result. The molecular finding establishes detection of M. tuberculosis complex in CSF; it does not by itself prove the mechanism of the extensive demyelinating lesions, which may represent ADEM-like inflammation, TB-related CNS injury, vasculitic injury, or overlapping pathology.

Treatment and clinical course

The initial working diagnoses were complicated pyogenic meningitis and possible cerebral malaria. Treatment included intravenous ceftriaxone and vancomycin, intravenous artesunate, and supportive care. After neurological review, ADEM was considered, and intravenous methylprednisolone 1 g daily for three days was administered. Acyclovir and sodium valproate were also given. The supplied treatment summary indicates that ceftriaxone and vancomycin were continued during the acute phase and later discontinued by the clinical team. Acyclovir was started empirically and was subsequently given by intravenous and oral routes according to clinical status; exact stop dates and total duration were not available in the supplied medication record.

As the patient deteriorated, the working diagnoses included complicated meningitis with possible vasculitis, ADEM, severe hyponatremia, and hypokalemia. Increased intracranial pressure was suspected, and head elevation and mannitol were prescribed. Antituberculous medications with pyridoxine were initiated during the admission when TBM and possible disseminated tuberculosis were considered. The supplied records do not establish the exact start date or provide a complete drug-by-drug antituberculous regimen. During the intensive-care course, dexamethasone was also initiated for complications associated with suspected raised intracranial pressure, but its precise dose and taper schedule were not available. The CSF GeneXpert MTB/RIF result detected M. tuberculosis complex, with rifampicin resistance not detected.

On the third day of stroke-ward admission, he developed worsening consciousness, severe desaturation despite oxygen by face mask, and diffuse bilateral coarse crackles. The treating team suspected mixed respiratory failure due to massive aspiration, with possible raised intracranial pressure and severe hyponatremia. He was transferred to the medical intensive care unit, intubated, and mechanically ventilated. During ICU admission, he remained comatose and required ongoing antimicrobial, antituberculous, corticosteroid, electrolyte, and supportive treatment. The notes document use of vasopressor support during the terminal course.

Sodium improved to 120.7 mmol/L and subsequently 134 mmol/L, after which salt replacement was discontinued in the documented plan. In contrast, hypokalemia worsened despite replacement, reaching 2.13 mmol/L. During the ICU course, spontaneous breathing and central and peripheral pulses ceased. Cardiopulmonary resuscitation was performed, and return of spontaneous circulation was achieved after six cycles. Intravenous potassium replacement and vasopressor support continued. The patient remained profoundly neurologically impaired, with a subsequent GCS recorded as 2T/15 and fixed, dilated pupils.

Outcome and documented cause of death

The official death summary recorded death on 22/10/2018 E.C., after a total hospital stay of seven days and on the fifth day of MICU admission. The recorded immediate cause was multiorgan failure

secondary to refractory septic shock attributed to severe bilateral aspiration pneumonia. Increased intracranial pressure and severe refractory hypokalemia were recorded as intervening or contributory conditions. The underlying neurological condition was recorded as triplegia secondary to ADEM with CNS vasculitis, with presumptive disseminated tuberculosis/TBM and an initial mixed malaria infection listed as initiating or contributory conditions.

The death summary's causal attribution is reproduced as the treating team's documented assessment. The supplied material does not include autopsy findings or microbiological confirmation of the suspected aspiration pneumonia, and therefore the relative contribution of sepsis, neurological injury, post-arrest injury, and severe hypokalemia cannot be independently established from the available documentation.

Discussion

This case demonstrates a rapidly progressive and fatal CNS illness in an adult with both microbiologically supported TBM and imaging findings interpreted as highly characteristic of ADEM. The initial febrile syndrome, headache, behavioral change, seizures or seizure-like episodes, progressive limb weakness, urinary retention, and sensory level indicated a serious encephalopathic and myelopathic process. The MRI showed extensive asymmetric cerebral white matter abnormalities and longitudinally extensive transverse myelitis, while CSF testing identified M. tuberculosis complex. The most defensible interpretation is therefore TBM with extensive demyelinating or ADEM-like CNS lesions; the precise pathophysiological relationship between infection and demyelination remains uncertain.

ADEM is usually diagnosed from the combination of acute encephalopathy, multifocal neurological deficits, compatible MRI lesions, and exclusion of better explanations. Large, poorly marginated, asymmetric T2/FLAIR lesions with deep and subcortical white matter involvement can support ADEM. However, the presence of leptomeningeal enhancement, a markedly inflammatory CSF profile with low glucose, and positive CSF GeneXpert strongly supports concurrent TBM. Tuberculous meningitis can cause basal meningeal inflammation, vasculitis, infarction, hydrocephalus, and other neurological complications. Consequently, the imaging cannot be interpreted as proof that ADEM alone caused the neurological syndrome. [1, 2, 6, 7]

The long-segment spinal cord lesion and sensory level at the umbilicus were consistent with longitudinally extensive transverse myelitis. Such a finding can occur in inflammatory demyelinating disease, including ADEM-like presentations and MOG antibody-associated disease, but infectious myelitis and TB-related inflammation must also be considered. The supplied record does not include serum MOG-IgG or AQP4-IgG results, nor does it provide tissue pathology. These missing data prevent further classification of the demyelinating process. [1, 2]

The initial malaria infection is also clinically relevant. The supplied records report mixed P. falciparum and P. vivax infection before referral, residual P. falciparum parasitemia on hospital presentation, and subsequent negative smears after intravenous artesunate. This sequence supports a marked reduction

in detectable parasitemia during treatment. However, the records alone cannot prove that all later organ dysfunction was entirely attributable to TBM or ADEM, nor can they exclude malaria as a contributor to the initial illness. The neurological decline despite falling parasitemia should prompt consideration of concurrent CNS disease rather than assuming that malaria alone explains the clinical course. [8]

Severe hyponatremia was another major complication, with sodium reaching 111.9 mmol/L. CNS infection, including TBM, can be associated with hyponatremia through several mechanisms, including SIADH and cerebral salt wasting. Distinguishing these conditions requires clinical volume assessment and relevant serum and urine studies. Although the supplementary material proposes SIADH, the necessary diagnostic measurements were not provided; this mechanism should therefore be described as suspected rather than confirmed. The records show that sodium subsequently normalized, but the exact rate of correction and its relationship to neurological status cannot be determined. [9, 10]

Profound hypokalemia persisted and reached 2.13 mmol/L despite supplementation. Severe hypokalemia can cause muscle weakness and predispose to arrhythmias, but the available documentation does not establish that it directly caused the cardiac arrest. The arrest occurred in the setting of critical illness, respiratory failure, suspected aspiration pneumonia, and severe neurological dysfunction. The timing of potassium measurements and replacement, ECG findings, magnesium levels, and rhythm during arrest would be needed to assess its contribution more confidently.

The clinical course highlights the difficulty of balancing immunotherapy for suspected ADEM with treatment of active CNS infection. High-dose corticosteroids are commonly used for severe ADEM, whereas TBM requires prompt multidrug antituberculous therapy and careful management of complications. In this case, empiric antibacterial and antiviral treatment, antimalarial therapy, corticosteroids, and subsequently antituberculous treatment were administered as the differential diagnosis evolved. The supplied records do not allow a conclusion about whether the timing of any individual therapy changed the outcome. [3, 5, 7, 11]

The fatal outcome was attributed in the official death summary to multiorgan failure following refractory septic shock associated with severe aspiration pneumonia, with raised intracranial pressure, severe hypokalemia, TBM, and ADEM with CNS vasculitis recorded as contributory or underlying conditions. This should be reported as the documented clinical attribution rather than as a cause independently verified by autopsy. Severe encephalopathy, impaired airway protection, aspiration, and respiratory failure formed a plausible sequence of deterioration, but the relative contributions of infection, CNS inflammation, metabolic disturbance, and post-cardiac-arrest injury remain uncertain.

Strengths and limitations

A strength of this case is the availability of serial clinical observations, brain and spinal MRI descriptions, CSF biochemistry and cell counts, and a positive CSF GeneXpert MTB/RIF result with rifampicin resistance not detected. These data support TBM and document extensive CNS involvement.

Important limitations remain. The report relies on retrospective clinical documentation, and the exact start dates and total durations of several treatments—including antituberculous therapy, artesunate across referral settings, ceftriaxone, vancomycin, and acyclovir—could not be reconstructed fully from the available summaries. The exact antituberculous drug regimen and the dexamethasone dose/taper were not supplied. Serum and urine osmolality, urine sodium, magnesium levels, ECG or cardiac rhythm during arrest, a complete chest imaging report, MOG-IgG/AQP4-IgG results, and autopsy findings were not available. TBM is supported by positive CSF GeneXpert, while ADEM remains a clinical-radiological interpretation rather than a histopathologically confirmed diagnosis. The cause of death is reported according to the official clinical death summary.

Conclusion

This fatal case illustrates the diagnostic complexity of extensive cerebral and spinal cord lesions in an adult with CSF GeneXpert-confirmed tuberculous meningitis and concurrent mixed malaria infection. MRI findings were considered highly characteristic of ADEM, but the inflammatory CSF profile and molecular detection of M. tuberculosis require the case to be interpreted as TBM with an ADEM-like demyelinating or inflammatory process, without claiming that the mechanism of the lesions is definitively established. The course was complicated by severe hyponatremia, refractory hypokalemia, suspected aspiration pneumonia, respiratory failure, cardiac arrest, and refractory septic shock. The case emphasizes parallel investigation and treatment of infectious and inflammatory CNS disease, close electrolyte monitoring, and early critical-care support.

Declarations

Ethical Approval

Not applicable

Consent for Publication

Written informed consent was obtained from the patient immediate kin for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Competing Interest

None

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Author Contribution

KTY: management of the patient, wrote the original draft, and revision of the final manuscript, Supervision

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Not Applicable

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