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Case Report

Acute Acalculous Cholecystitis Associated with Severe Malaria – A Case Report

Teresa Oliveira [1,*], **Ana Clara Dinis** [2], **Sofia Narciso** [1], **Tiago Pereira** [1], **Nuno Catorze** [1]

[1] Intensive Care Medicine Service, Médio Tejo Local Health Unit, Abrantes, Portugal.
[2] Internal Medicine Department, Médio Tejo Local Health Unit, Abrantes, Portugal.

* Correspondence: mariateresa.oliveira@ulsmt.min-saude.pt.

Abstract: We present the case of a 29-year-old male diagnosed with severe malaria admitted to the Intensive Care Medicine Service. While undergoing treatment with quinine dihydrochloride and doxycycline, he developed an acute case of acalculous cholecystitis on the fourth day. Conservative treatment with antibiotic therapy was performed, and the patient showed favorable progression. Gastrointestinal complications associated with malaria are common; however, acute acalculous cholecystitis linked to malaria is an extremely rare complication, scarcely described in the literature, and its evolution can be catastrophic.

Keywords: Severe Malaria; Acalculous Cholecystitis; Case Report.

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1. Introduction

Acute Acalculous Cholecystitis (AAC) is a rare pathology, accounting for only about 10% of acute cholecystitis cases. It is more prevalent in male individuals over the age of 50 [1]. While its occurrence associated with severe sepsis has been previously described [2], it remains a rare condition as a complication of severe malaria, with very few cases reported in the literature [3]. Diagnosing AAC continues to be challenging, as it usually occurs as a secondary event in patients with another acute illness, reducing the sensitivity and specificity of clinical manifestations. Early diagnosis and treatment of AAC are crucial to prevent potentially fatal complications, such as gallbladder perforation and gangrene [1]. For these reasons, the authors considered it important to present and describe this case to raise awareness of this association.

Here, we present a case of severe *Plasmodium falciparum* malaria that developed into acute acalculous cholecystitis on the fourth day of hospitalization.

2. Case Report

A 29-year-old Black male, born and residing in Angola, had been on vacation in Portugal for 10 days. He presented to the Emergency Department of the Médio Tejo Hospital Center with complaints of fever, asthenia, anorexia, and generalized myalgia lasting four days. On the last day, he also reported bifrontal headache and diffuse abdominal pain. No other associated symptoms were noted. He had no relevant medical history or regular medications.

On admission, the patient was described as alert, cooperative but with slowed and sometimes confused speech, without focal neurological deficits; he was eupneic in room air with a peripheral oxygen saturation of 99%; blood pressure of 88/52 mmHg; heart rate

of 115 bpm; subfebrile with a tympanic temperature of 37.9°C; icteric sclerae; dehydrated; without abnormalities on cardiac or pulmonary auscultation; abdomen soft and depressible, with discomfort upon palpation in the upper quadrants and apparent hepatomegaly (liver palpable 3 cm below the right costal margin).

Laboratory findings (Table 1) revealed thrombocytopenia, elevated C-reactive protein (CRP), acute kidney injury, cholestatic liver injury, and hyperlactatemia. Chest X-ray showed no abnormalities, and a cranial computed tomography scan was unremarkable. Thick blood smear revealed 25% parasitemia, and antigen testing confirmed the presence of *Plasmodium falciparum*.

Table 1. Serial laboratory parameters.

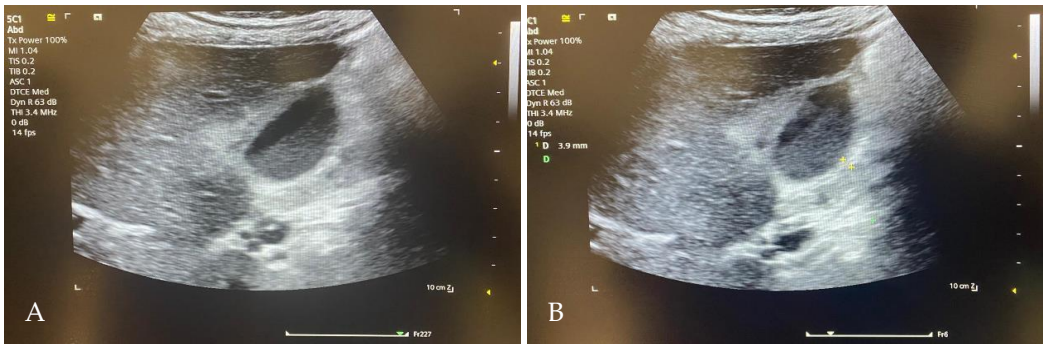
Parameter	Emergency Department	D1	D4	D8	D13
Hb (g/L)	14.2	12.1	6.9	7.5	9.8
Leukocytes	8,760	9,870	21,680	14,760	9,860
Platelets	6,000	22,000	32,000	68,000	142,000
Parasitemia (%)	25	22	5	>0.1	>0.1
CRP (<3 mg/dL)	26.6	18.2	24.2	16.4	4.2
Procalcitonin (<1.5 ng/mL)	62.8	43.1	58.2	12.8	0.9
Creatinine (0.8-1.2 mg/dL)	3.0	3.4	3.7	2.4	1.8
Urea (17-43 mg/dL)	115	135	150	110	78
Albumin (3.5-5.2 g/dL)	2.1	2.4	2.4	2.9	3.2
Amylase (28-100 U/L)	20	-	16	-	-
ALT/TGP (UI/L)	66	110	360	142	46
AST/TGO (UI/L)	125	122	320	136	40
GGT (UI/L)	293	315	942	235	112
ALP (30-120 UI/L)	120	180	325	246	152
LDH (UI/L)	805	940	1252	525	218
Total Bilirubin (0.3-1.2 mg/dL)	21.9	22.4	24.4	11.7	3.4
Direct Bilirubin (mg/dL)	18.6	19.7	21.0	8.7	1.9

Severe malaria was diagnosed according to WHO criteria [4], and the patient developed multi-organ dysfunction, including cerebral (Glasgow Coma Scale-GCS 13), cardiovascular (requiring vasopressor support), renal (non-oliguric), hepatic, and hematologic involvement. The patient was admitted to the Intensive Care Unit (ICU) for monitoring and appropriate therapy with quinine dihydrochloride and doxycycline.

During the ICU stay, after stabilization and supportive care, the patient showed progressive clinical improvement. On the fourth day of hospitalization, the patient developed fever (maximum tympanic temperature of 39.0°C) with associated abdominal discomfort, localized pain in the right hypochondrium, and a positive Murphy's sign, symptoms and findings highly suggestive of cholecystitis. Microbiological screening (blood cultures, urine cultures, and repeated SARS-CoV-2 testing) was performed, and Piperacillin/Tazobactam was empirically initiated.

Chest X-ray remained unremarkable; however, abdominal ultrasound (Figures 1A and 1B) showed gallbladder distension with wall thickening, with no evidence of gallstones. Consequently, acute acalculous cholecystitis associated with malaria was diagnosed, and General Surgery was consulted. A multidisciplinary team decision, involving General Surgery and Intensive Care, opted for conservative management, maintaining antibiotic therapy and close monitoring.

Figure 1. A and B. Abdominal ultrasound – gallbladder distension with wall thickening.



On the seventh day of hospitalization, despite improvement in abdominal symptoms, the patient developed progressively worsening dyspnea with exertion and gradually increasing hypoxemia, requiring non-invasive ventilation and, subsequently, orotracheal intubation and invasive mechanical ventilation. A chest X-ray revealed a pattern consistent with ARDS, which was confirmed by chest computed tomography (evidence of bilateral pleural effusion and ground-glass opacities). Following supportive treatment, fluid balance optimization, and positive pressure ventilation (invasive mechanical ventilation), the patient experienced hemodynamic stabilization and progressive clinical, analytical, and radiological improvement. He was extubated to oxygen therapy on the 11th day of hospitalization and transferred to the Internal Medicine ward on the 15th day.

During his ICU stay, the patient required sedation and invasive mechanical ventilation for four days, vasopressor support with norepinephrine for five days, and intermittent transfusional support with two units of packed red blood cells. While in the Internal Medicine ward, the patient continued to show favorable clinical progress without significant complications and was discharged on the 22nd day of hospitalization with a follow-up appointment in Internal Medicine.

3. Discussion

Acute acalculous cholecystitis (AAC) has been described in association with various infectious conditions, including those caused by *Leptospira spp., Salmonella spp., Vibrio cholerae, Coxiella burnetii*, dengue virus, *varicella-zoster* virus, *cytomegalovirus, Epstein-Barr* virus, hepatitis A virus, and, less frequently, *Cryptosporidium spp., Candida spp.*, and *Plasmodium falciparum*. A PubMed search over the past 15 years identified six articles describing cases of AAC associated with P. falciparum in both adults and children, highlighting the rarity of this condition worldwide [3, 5-9].

According to the WHO, in 2023, the African region accounted for 94% of malaria cases (246 million) and 95% (569,000) of malaria-related deaths [10]. Portugal has a significant number of immigrants from the African continent. Therefore, in patients presenting to the Emergency Department with nonspecific complaints such as headache, vomiting, abdominal pain, or diarrhea, and who have recently returned from Africa, a high index of suspicion for malaria is essential. Patients from highly endemic regions (where Plasmodium falciparum predominates) have increased exposure and are consequently at higher risk of severe malaria complications, including AAC. Although certain genetic traits common in individuals of African descent (e.g., sickle cell trait, G6PD deficiency) provide partial protection against severe malaria, they do not necessarily protect against AAC, which is more related to systemic inflammatory responses and ischemia than to parasitic action [11, 12].

The pathophysiology linking AAC and malaria remains unclear; however, mechanisms such as bile stasis/viscosity caused by fever and dehydration, impaired gallbladder perfusion due to ampullary spasms, and endotoxemia/ischemic damage from microangiopathy seem to be involved and associated with parasitemia [12]. Given the overlapping

clinical manifestations of malaria and AAC, a high diagnostic suspicion is crucial. Abdominal ultrasound is the diagnostic modality of choice, with a sensitivity and specificity of 50–100% [13]. Diagnostic criteria include gallbladder distension, a positive Murphy's sign, wall thickening >3 mm, and pericholecystic fluid, in the absence of gallstones—favoring the diagnosis when at least two criteria are present. In this case, all criteria were met.

As with other reported cases, the clinical course was favorable without the need for surgical intervention, relying on medical management with supportive measures, antibiotics, and antimalarial therapy. In certain cases, percutaneous transhepatic gallbladder drainage is described as a safe and effective alternative to surgery, particularly in high-risk patients with severe underlying medical conditions and significant clinical instability.

4. Conclusion

Although rare, AAC can be a complication of severe malaria. While gastrointestinal manifestations associated with malaria are not uncommon, AAC remains a rare, potentially under-recognized condition that can have severe consequences if not promptly diagnosed and treated. First, it is essential to maintain a high index of suspicion for malaria in patients returning from endemic regions. Second, in cases involving hepatic abnormalities and abdominal pain, AAC should be considered and excluded. Early diagnosis through imaging and timely initiation of appropriate therapy are critical for achieving a favorable outcome for the patient.

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Research Ethics Committee Approval: We declare that the patient approved the study by signing an informed consent form and the study followed the ethical guidelines established by the Declaration of Helsinki.

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Conflicts of Interest: The authors declare no conflicts of interest.

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