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Serendipity in Emergency Diagnostics: Near Miss of a *Loa loa* Case in a Swiss Hospital

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ABSTRACT

A 31-year-old Cameroonian man presented to the emergency department (ED) with a productive cough, exertional dyspnoea, and asthenia for a few days. The initial evaluation was limited due to cultural barriers, lack of known medical history, and the patient's migration journey through Libya, Tunisia, and Germany over the past 5 years before recently arriving in Switzerland. Clinical examination revealed no red flags. Blood counts were normal, C-reactive protein (CRP) was elevated at 91 mg/L, and a chest X-ray was unremarkable. A diagnosis of influenza-like syndrome was made. The patient returned the following day with increased fatigue and fever. A rapid malaria test was negative, a blood smear was ordered, and CRP levels rose to 148 mg/L. During an influenza epidemic, PCR confirmed Influenza A. The patient was reassured and prescribed ibuprofen and paracetamol. Subsequently, the laboratory detected not malaria but filariae, and a diagnosis of Loiasis (*Loa loa*) was established. The patient was referred for specialist consultation. Treatment with albendazole was initiated, leading to gradual improvement.

1 | Introduction

Loiasis is a filariasis caused by *Loa loa*, also known as African eye worm, transmitted by blood-sucking flies and endemic in Central Africa and parts of West Africa, with the highest prevalence reported for rural regions of Equatorial Guinea, parts of Cameroon, the Central African Republic, the Democratic Republic of the Congo, Republic of the Congo, and Gabon. Until recently, Loiasis was considered a benign disease by local communities in these regions, which has led to the disease being completely neglected by local health systems and international health organizations. However, recent studies have shown an excess of mortality in patients with Loiasis as well as an increase in morbidity in this sub-group of patients, underlining the burden of this disease and the need to diagnose and treat it [1–3]. The World Health Organization developed the RAPLOA tool to rapidly assess *Loa loa* endemicity in African communities [4]. A recent systematic review further highlighted the complex interplay between *Loa loa* transmission and environmental and human factors that challenge accurate diagnosis [5].

Loa loa larvae are transmitted to humans through the bite of chrysops. They mature within the wound until they become adult worms, then migrate to the subcutaneous and fascial layers where they reproduce and give rise to multiple microfilariae, which are then found in the peripheral blood before being

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Summary

- Cognitive biases are inherent in medical reasoning and can lead to errors, occurring often when the required knowledge is lacking or in emergency situations, rushing the clinical reasoning.
- Doctors must be aware of their cognitive biases to minimize their impact on their everyday practice.

ingested by a chrysops during a future bite. The incubation period between the transmission of larvae and the appearance of the first clinical symptoms is 3–6 months, with an average delay of 1 year for the appearance of microfilariae in the peripheral blood. Signs and symptoms vary from person to person. Typically, the adult worm's eponymous migration through the sclera or palpebral subconjunctival tissue can cause intense pain, signs of inflammation, and a pruritic swelling. Other classic signs include swelling of the wrist, known as "Calabar swelling" and superficial migration of the worms through the subcutis. In addition to the classic signs specific to Loiasis, patients also report asthenia, severe headaches, arthralgias, and myalgias, as well as generalized pruritus and rashes. Complications are rare but clinically important, as potentially life-threatening, and are thought to be associated with high levels of microfilariae in the blood. They include loss of vision, encephalitis, nephropathy, cardiomyopathy, pulmonary inflammation, and septic arthritis. The standard diagnosis is based on the identification of worms by light microscopy on a blood smear stained with Giemsa or hematoxylin, although sensitivity depends on the quantity of blood examined. Molecular detection of microfilariae has recently been added to the diagnostic options, demonstrating good sensitivity and high specificity, as has anti-loa-loa antibody serology. Treatment is based on the administration of albendazole for at least 4 weeks until the microfilariae count is below 2000 microfilariae per ml, followed by the administration of diethylcarbamazine in 21-day cycles until cured (40%–80% cure rate per cycle) [1, 2, 6].

The increasing number of migrants has resulted in more emergency consultations. Cultural and linguistic barriers can hinder access to care, lead to discriminatory attitudes based on stereotypes, and increase the risk of errors [7]. These phenomena are exacerbated by stress and the urgent nature of emergency medicine [7]. Moreover, the growing number of migrants from disease-endemic areas is bringing pathologies that were previously little known to Europe, and especially to Switzerland, increasing the risk of misdiagnosis, as we look first for what is common and known [3]. This case study reports a near miss of a *Loa loa* disease in a Cameroonian patient seeking asylum and aims to explore the pedagogical potential and analyze the medical reasoning involved.

2 | Case History/Examination

A 31-year-old Cameroonian patient seeking asylum, in good health as usual, presented to the emergency department (ED) for the first time with severe asthenia and a productive cough with haemoptysis for about 2 days, with a deterioration in general condition despite taking paracetamol. He also reported diffuse chest pain when coughing, a sensation of dyspnoea when lying supine, and a feverish feeling. In his migration history, he stated that he had been in Switzerland for 4 months and had migrated via Tunisia and Libya, where he stayed for 1 year before reaching Europe. He stayed in Europe for a few years before reaching Switzerland. The history of contagious influenza symptoms is positive in the household where he lives. The rest of the history, including family and psychosocial history, was unremarkable. He also declared no relevant past interventions or surgeries. The patient was haemodynamically stable, had no fever, and there were no abnormalities in his cardiovascular, pulmonary, or abdominal clinical status. Influenza-like syndrome was suspected, and the patient was discharged home with symptomatic treatment and a proposal for biological monitoring of the inflammatory syndrome after 48 h.

He went back to the ED that evening because of general weakness, insomnia, and new-onset dizziness with nausea but no vomiting and odynodynophagia. He did not present with any new haemoptysis. The clinical status was like that of the first consultation, with no fever and an unremarkable neurological status. The back of the throat was normal, and there were no palpable cervical or axillary adenopathy. The patient was again sent home with a prescription for an herbal sleeping pill (Redormin).

He presented to the ED for the third time 2 days later because of the appearance of green vomiting and the recurrence of coughing with brown to black sputum. He also reported a drop in thymine, anemia, and intermittent suicidal ideation in the absence of auditory or visual hallucinations. The rest of the history by system was unremarkable, in particular no chills or fever. Clinical status revealed a slightly tender abdomen in the left iliac fossa, with palpation of stools, and a slightly erythematous back of the throat. The rest of the clinical status was unremarkable. The patient was sent home with a diagnosis of influenza A and symptomatic treatment.

3 | Differential Diagnosis, Investigations and Treatment

On his first visit to the ED, the biological tests showed an elevated CRP (91 mg/L) with no leucocytosis (9.1 G/L), and no other abnormalities were detected, specifically no haemolytic anemia or thrombocytopaenia. The ECG was unremarkable, as was the chest X-ray, which showed no suspicious opacities. Upon the second visit to the ED on the same day, the investigations were extended with a rapid test for malaria, which came back negative.

On his third visit to the ED, the laboratory work-up was repeated and revealed an increased inflammatory syndrome with a CRP of 148 mg/L with no leucocytosis (6.5 G/L) and a normal procalcitonin (0.11 mcg/L). Liver, pancreatic, and renal function were normal. A nasopharyngeal swab came back positive for influenza A and negative for influenza B, COVID-19, and RSV. A second rapid test for malaria was also negative, but to complete the work-up in view of the patient's persistent symptoms and migratory history, a blood smear analysis and serology for Plasmodium sp. were requested.

4 | Outcome and Follow-Up

The malaria serology came back positive, which in view of the negative rapid test, speaks against active malaria. Analysis of the blood smear showed the presence of microfilariae (Figure 1) which, after identification by the national centre for imported parasitic diseases, turned out to be *Loa loa* microfilariae. The thick blood smear, stained with Giemsa, was performed twice. The first time during the night (2 a.m.), the second one during the daytime (early morning), which serendipitously aligned with the known diurnal periodicity of *Loa loa*. No concentration techniques were necessary, as the parasitaemia (4413 microfilariae/mL) was sufficient for direct visualization under light microscopy.

Treatment with Albendazole 400 mg twice daily for 4 weeks was initiated with a gradual improvement in symptoms. During follow-up consultations, the patient stated that he was taking his treatment meticulously and did not mention any significant side effects, even after specific questioning. Biological monitoring did not show any alteration of liver function. After the 4-week treatment regimen, the microfilariae concentration was less than 2000/mL, allowing for curative treatment with diethylcarbamazine (DEC) at a rate of 9 mg/kg three times a day for a 21-day cycle. After 2 cycles of DEC, the patient's microfilariae were undetectable in the peripheral blood. The patient also did not mention any significant side effects during the DEC cycles. No treatment adjustment was necessary during the entire follow-up period.

During the follow-up consultations, the patient expressed his gratitude for the care and treatment provided and the close follow-up offered, which he would not have had access to in his country of origin. He understands that his ethnic origin may have influenced the reasoning behind his illness and that the language difficulties, as he does not speak French or German well, probably contributed to the diagnostic wandering, but insisted that he did not feel less welcome, listened to, or cared for as a result. Although these symptoms seemed mild, he felt reassured to always have the option of returning to the ED if his symptoms did not improve, which ultimately led to the correct diagnosis being made. Adhering to the treatments was not easy for him, given the need to take two then three tablets a day, and he is grateful for the support provided during follow-up consultations with the infectiologist and his general practitioner. He also felt lucky to tolerate the treatment well and finally achieve a cure for his disease.

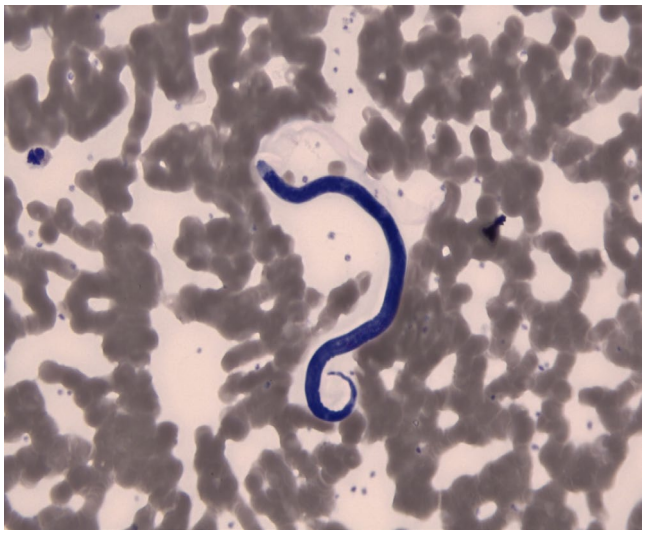

FIGURE 1 | *Loa loa* microfilaria, Light Microscopy. Thick blood drop smear showing a *Loa loa* microfilaria, light microscope, Giemsa stain. Magnification 100× (photo: laboratory Department, University and Teaching Hospital, Fribourg, Switzerland).

5 | Discussion

We report here the case of a Loiasis whose diagnosis was only made incidentally at the end of the third consultation while investigating for malaria and, in so doing, we aim to analyze the medical reasoning involved and the associated educational potential. To do so, it is first necessary to explore how medical reasoning works from a theoretical point of view [7–9]. In recent years, there has been a growing focus on the thought processes involved in clinical decision-making, which have major consequences for patients. The predominant theory about clinical reasoning involves a dual cognitive process [8]. Type 1 reasoning is intuitive, almost unconscious, and very rapid, creating direct associations between situations and cognitive scripts based on prior knowledge. Beneficial and coming into its own in situations requiring quick decision-making, such as encountered in emergency medicine, it is, however, clearly influenced by our cognitive and affective biases (e.g., intrusion of prejudices and emotional factors), inherent to the environmental and human factors. Type 2 reasoning involves structured acquisition and analytical data processing to establish a differential diagnosis [8, 9]. Slower and more objective, it is less at risk of being influenced by the aforementioned elements.

A second important concept involved in medical reasoning and diagnostic performance is the relationship between signal and noise, or in other words, the extent to which the signs and symptoms (signal) are pathognomonic of the pathology or, on the contrary, common to multiple diseases (noise). The more characteristic or even pathognomonic the signs and symptoms of the disease, the higher the diagnostic performance, even in the case of intuitive reasoning (Type 1). On the other hand, the more nonspecific the signs and symptoms are, the broader the differential diagnosis, the poorer the diagnostic performance in the context of intuitive reasoning (Type 1) and the more data and time analytical reasoning (Type 2) will be required to reach a diagnosis [9].

The patient presented to the ED with Influenza-like symptoms during the period of the influenza epidemic. This non-specific clinical presentation, or in other words, with a low signal-to-noise ratio, consistent with the current flu epidemic, probably disrupted intuitive reasoning due to a probability bias and consequently obscured the other differential diagnoses [10]. This situation also illustrates an anchoring bias, where the initial presentation anchored clinical reasoning around a common viral diagnosis, delaying the consideration of alternative aetiologies such as parasitic infections [11]. The investigation for malaria may be criticized, given that the patient had been in Europe for several years and showed no fever, splenomegaly, haemolytic anemia, or thrombocytopenia, and is probably the corollary of the patient's ethnic origin [12]. The inflammatory syndrome was correlated with a positive Influenza A

TABLE 1 | Interpretation of biomarkers in the context of an infectious syndrome.

Biomarkers	Normal values	Viral etiology	Bacterial etiology	Parasitic etiology
Leukocytes	< 10 G/L	Generally normal	Elevated	Normal
Lymphocytes	20%–40% or 1–4 G/L	Normal, sometimes elevated, presence of atypical lymphocytes	Normal, sometimes elevated	Normal
Eosinophils	< 0.5 G/L	Normal	Normal	Elevated if helminths
Left Shift	> 1 G/L or > 25%	Normal or elevated (acute phase)	Elevated, especially in the acute phase	Normal
CRP	< 5 mg/L	Normal or slightly elevated	Elevated	Variable
PCT	< 0.5 µg/L	Normal or slightly elevated	High	Normal

Note: Useful (non-exhaustive) biomarkers and indicative interpretation to aid in diagnosing infectious syndromes. To be interpreted in the clinical context, as these biomarkers do not have sufficient sensitivity and specificity to confirm or exclude a diagnosis reliably.
Abbreviations: CRP, C-reactive protein; PCT, procalcitonin.

PCR result during an influenza epidemic, although quite high for a viral origin (Table 1) [13, 14]. This probably stemmed from a confirmation bias, i.e., the information was processed to confirm the diagnostic hypothesis and not objectively [15]. The elevated CRP levels, as observed in this patient (91 and 148 mg/L), should have prompted consideration of a broader differential diagnosis, including bacterial or parasitic infections or vasculitis, even though some studies indicate CRP lacks specificity for predicting infections or guiding appropriate therapeutic choices [13, 14, 16].

On his third visit to the emergency room, although the inflammatory syndrome was worse, the broadening of the differential diagnosis was probably again skewed by the confirmation bias (performance of a nasopharyngeal swab that came back positive for flu) as well as by the patient's ethnic origin (repeat of the rapid test, then request for analysis of the blood smear as well as serology tests for malaria) [15]. It is however noteworthy that this ultimately led to the incidental diagnosis of Loiasis. The initial cough was most likely unrelated to *Loa loa* infection and better explained by the concurrent influenza A infection, confirmed by PCR. Nonetheless, eosinophilic pulmonary manifestations have occasionally been reported in Loiasis, particularly in cases of high microfilaremia.

Recent studies demonstrate how gender and ethnicity affect diagnostic variability [17, 18]. Compared to white patients, Black patients are less likely to receive emergency treatment for the same complaints. Similarly, women are less likely than men to receive equitable treatment. Biases are more frequent among practitioners with higher workloads or patient volumes. Such unconscious attitudes impact the patient-doctor relationship, reduce adherence to treatment, and lower patient satisfaction. They also perpetuate negative assumptions about compliance and ultimately influence care delivery [19].

Ongoing debate exists on whether cognitive biases linked to human factors can be prevented. Evidence suggests that slowing cognitive processes, using metacognition, and applying checklists may be helpful but insufficient to eliminate diagnostic errors. We remain prone to errors inherent in our cognitive processes, especially when knowledge is limited [8, 15].

Through this case report, we wish to emphasize 2 learning points. First, biases are inherent to medical practice, and we must remain cautious to limit their impact on our clinical reasoning process. Knowledge of these cognitive biases and the simple strategies for minimizing their respective impacts in everyday clinical practice must be taught and integrated into continuing education programs for healthcare services [11]. Second, Loiasis, a common disease in Central Africa where it is endemic [2], can also be encountered in Europe, especially with the increase in patients who have migrated from these endemic regions.

Author Contributions

Azad Durussel: conceptualization, data curation, formal analysis, investigation, methodology, project administration, validation, visualization, writing – original draft, writing – review and editing. **Sébastien Pugnale:** conceptualization, data curation, formal analysis, investigation, methodology, project administration, validation, visualization, writing – original draft, writing – review and editing. **Ludovic Galofaro:** conceptualization, data curation, methodology, project administration, resources, software, supervision, validation, writing – original draft, writing – review and editing. **Jean-Luc Magnin:** formal analysis, methodology, resources, visualization. **Youcef Guechi:** funding acquisition, methodology, resources, supervision, validation, writing – original draft, writing – review and editing. **Vincent Ribordy:** conceptualization, funding acquisition, project administration, resources, supervision, validation, writing – review and editing.

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Ethics Statement

Ethics committee approval was not required for this case report in accordance with the institutional policies, as it presents a single anonymized patient case with informed consent.

Consent

Patient consent to publish clinical information and images was obtained in written form using a consent form in French. The patient has agreed to the terms outlined in Wiley's standard consent form, including

understanding that their medical information will be published on an open access basis and may be freely accessed worldwide.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors have nothing to report.

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