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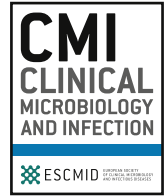
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Letter to the Editor

No evidence for major adverse events related to suspicion of Ebola in France, 2014–2015

Ebola virus is one of the most virulent human pathogens, mostly transmitted by direct contact through broken skin or mucous membranes with blood or blood-contaminated body fluids. The 2014–2015 Ebola virus disease (EVD) outbreak in West Africa—by far the largest in history to date—has affected more than 28 500 patients and has killed more than 11 000. Outside of the outbreak area, most countries implemented surveillance systems and specific rules for the management of suspect cases to ensure that no secondary transmission occurs. Patients were classified as having suspected EVD if they presented with fever within 21 days after leaving an area at risk.

The importance of these precautions has been outlined by reports of secondary transmission in Spain [1] and the United States [2], when they were not adequately implemented. However, most suspicion of EVD outside of the outbreak area turned out to be more common infectious diseases, including malaria [3], and concerns were raised that EVD suspicion could represent a loss of opportunity for early recognition and treatment of these potentially life-threatening conditions. In addition, the use of Ebola personal protective equipment has been shown to increase the risk of failure for common medical procedures [4] and has psychological consequences. We aimed to characterize the management of patients suspected of EVD in France in 2014–2015, focusing on time elapsed between EVD suspicion, and final diagnosis and treatment.

We performed a retrospective multicentre study of suspected EVD cases managed in France from April 2014 to August 2015. Inclusion criteria were fever, stay in an Ebola outbreak area within 21 days before fever onset and hospital admission for EVD suspicion. The study was communicated to >700 physicians through the mailing list of the French infectious diseases society (Société de Pathologie Infectieuse de Langue Française (SPILF)). Data were extracted from medical charts by physicians in charge and collected on a standardized questionnaire, including timing of the following events: admission, isolation start and discontinuation, diagnosis, treatment and discharge. Diagnosis and treatment delays attributable to EVD suspicion were estimated through review of medical charts separately by at least two investigators (three, in case of discrepancy). The study was approved by the French institute for medical research and health institutional review board (approval 14–184).

Thirty-four patients fulfilled the inclusion criteria (19 male and 15 female subjects), with a median age of 33 years (interquartile range (IQR), 26–43). They returned from Guinea ($n = 21$), Nigeria ($n = 4$), Sierra Leone ($n = 3$), Mali ($n = 3$), Liberia ($n = 2$) and Congo ($n = 1$). For seven patients, fever onset occurred in the outbreak area; for the remaining 27, fever appeared in France, with a median

duration of 1 day (IQR, 0–8) between return and fever onset. Other symptoms included asthenia ($n = 27$), headache ($n = 20$), myalgia ($n = 18$), abdominal pain ($n = 10$) and diarrhoea ($n = 9$). The median duration between fever onset and admission was 1 day (IQR, 0–5), and the median duration of patient isolation with EVD specific precautions was 8 hours (IQR, 2–30). The final diagnosis was obtained in 28 patients (82%), with a predominance of *Plasmodium falciparum* malaria ($n = 10$; 29%). Retrospective review of medical files suggested that for 12 patients (35%), EVD suspicion was associated with a diagnosis delay (Table 1) for a median duration estimated at 3 hours (IQR, 2–36). The three cases with diagnosis delays estimated to be >12 hours were viral gastroenteritis (36 hours), non-severe malaria (50 hours) and influenza B (51 hours). All patients survived.

We found that most patients with suspected EVD in France during the 2014–2015 outbreak were finally diagnosed with other infectious diseases, mostly malaria, and none had EVD. This is in line with studies from the GeoSentinel Surveillance Network [3], with malaria documented in 40% of ill travelers returning from Sierra Leone, Liberia and Guinea. We estimated that a diagnosis delay attributable to EVD suspicion occurred in 35% of patients, but remained limited in most, with no major clinical consequence. However, delayed diagnosis and treatment of malaria attributable to EVD suspicion has been reported [5].

This study has limitations resulting from small sample size, potential bias related to retrospective collection of data and subjective

Table 1Differential diagnosis and treatment delay attributable to suspicion of Ebola virus disease ($n = 34$)

| Final diagnosis | Diagnosis delay attributable to EVD suspicion, n (%) | Time from admission to treatment initiation in patients with delay |
|--|--|--|
| Malaria ($n = 10$) | 6 (60%) | Median 2 hours (IQR, 0–10) |
| Community-acquired pneumonia ($n = 3$) | 1 (33%) | 2 hours |
| Gastroenteritis ($n = 3$) | 1 (33%) | No treatment |
| Influenza-like illness ($n = 2$) | 0 | No treatment |
| Pharyngitis ($n = 2$) | 1 (50%) | No treatment |
| Miscellaneous ($n = 8$) ^a | 3 (37%) | Pyelonephritis, 2 hours; epilepsy, 3 hours; influenza B, 51 hours |
| No final diagnosis, fever resolved ($n = 6$) | — | — |

IQR, interquartile range.

^a Cellulitis, pyelonephritis, tuberculosis, HIV, salmonellosis, shigellosis, influenza B, epilepsy (one patient each).

estimation of treatment delay. However, because participating centres were required to enroll all cases of suspicious EVD, this case series may be more representative of the actual adverse events related to the situation of suspicion of EVD compared to individual case reports. Of note, a consensus on treatment delay was reached through independent review of medical files by two investigators in all cases.

In conclusion, we found no evidence of major adverse events related to suspicion of EVD in France in 2014–2015, as most patients were adequately diagnosed and treated within the first hours after admission. However, the risk of adverse events related to suspicion of such highly pathogenic viruses must be taken into account in the design of guidelines for screening and management of suspect cases.

Transparency Declaration

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