Ebola Hemorrhagic Fever in Kikwit, Democratic Republic of the Congo: Clinical Observations in 103 Patients

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During the 1995 outbreak of Ebola hemorrhagic fever in the Democratic Republic of the Congo, a series of 103 cases (one-third of the total number of cases) had clinical symptoms and signs accurately recorded by medical workers, mainly in the setting of the urban hospital in Kikwit. Clinical diagnosis was confirmed retrospectively in cases for which serum samples were available ($n = 63$, 61% of the cases). The disease began unspecifically with fever, asthenia, diarrhea, headaches, myalgia, arthralgia, vomiting, and abdominal pain. Early inconsistent signs and symptoms included conjunctival injection, sore throat, and rash. Overall, bleeding signs were observed in <45% of the cases. Typically, terminally ill patients presented with obtundation, anuria, shock, tachypnea, and normothermia. Late manifestations, most frequently arthralgia and ocular diseases, occurred in convalescent patients. This series is the most extensive number of cases of Ebola hemorrhagic fever observed during an outbreak.

The 1995 outbreak of Ebola (EBO) hemorrhagic fever (EHF) in the Democratic Republic of the Congo (DRC) was the largest ever observed among humans in an urban center, where potential exists for much broader dissemination of the disease. The outbreak was caused by an EBO virus that was very similar to the one involved in Yambuku, DRC, in 1976 [1, 2]. The outbreaks were comparable in magnitude (316 and 318 cases, respectively) and had case-fatality ratios of ~80% [2, 3].

Epidemiologic surveys have shown retrospectively that cases occurred as early as January 1995 [4], but it was not until EHF was introduced into a hospital environment, where it affected a large number of health care workers, that the disease was suspected to be a viral hemorrhagic fever. Prompt notification of the situation to the World Health Organization by DRC health authorities and testing of patient samples at the Centers for Disease Control and Prevention led to the diagnosis of EHF on 10 May 1995 [5]. Within days, the international community dispatched scientific and rescue teams, who, with their DRC colleagues, had the opportunity to monitor the evolution of the outbreak at its peak, to make clinical observations, and to implement the appropriate containment measures. Herein, we present the analysis of clinical information for 103 patients; the information was recorded by medical personnel during the patients' hospitalization.

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Setting and Circumstances of the Study

Kikwit, a rural town located in Bandundu region, on the banks of the Kwilu River, has an estimated population of 400,000 inhabitants [6]. It lies at crossroads connecting Kinshasa (400 km to the west), the capital of DRC, to eastern DRC and to Angola in the south. Kikwit General Hospital, the main health care facility of the town, has a total capacity of 375 patients and consists of 12 separate one-floor pavilions, most of them designed for inpatient care, with a capacity of 36 beds each. A typical inpatient ward comprises two identical common rooms separated by a middle connecting area that provides access to four small rooms, which are used as private patient rooms, the nurses' office, or the storage area. Other pavilions house administrative offices and the pharmacy, the emergency room, the delivery room, two laboratories, the operating theater, and a radiography section. In ordinary times, the hospital staff comprises 12 physicians, ~200 nurses or midwives, and 60 room attendants.

By 9 May 1995, most of the routine activities of Kikwit General Hospital, with the exception of a few deliveries, had been suspended. New patients were still admitted in the emergency ward and, if their complaints were suggestive of EHF, they were examined in one of two separate rooms. When the diagnosis of EHF was considered probable, patients were directed to a single pavilion (Pavilion 3) designated as a quaran-

tine facility. Other patients were given essential care and sent home or transferred to another health center when surgery was required. By 12 May, patients in Pavilion 3 were attended by only 3 volunteer nurses and 1 physician. Several health care workers were among the hospitalized patients. Others were involved in the organization of emergency rescue or were unwilling to work in Pavilion 3 until safe conditions could be restored. Oral and parenteral drugs (including quinine, chloroquine, antibiotics, sedatives, and analgesics) were still supplied by the hospital pharmacy, but water and electricity were lacking. Sanitation was basically nonexistent, and deceased patients were no longer being evacuated from the quarantine area. As a rule, needles had not been reused between patients; however, needles and infusion sets were not disposed of in containers; thus, health care workers were at high risk for needlestick injuries, especially in the diminished lighting of the ward. Therefore, instructions were given to limit injections and infusions to a minimum and to encourage family attendants to provide maximal oral hydration to their relatives. Moreover, no laboratory facilities were in operation to monitor parenteral therapeutic interventions.

On 13 May, after an international team had arrived, the quarantine pavilion and the emergency room were restaffed, and sanitation work was started as protective equipment became available. By 20 May, enough nurses had volunteered for duty to allow the opening of an additional quarantine pavilion for patients when the capacity of Pavilion 3 was exceeded.

Despite these emergency circumstances, records were still kept for most of the patients, and minimal but sufficient clinical observations were registered either by the attending physicians or by the nurses. Available information typically included demographic data, symptoms on admission, body temperature, pulse, treatment, disease progression, and date of death. Extensive clinical examination was attempted only in a limited number of cases in the quarantine area because of time and safety limitations. In retrospect, fine discrimination of some recorded symptoms was judged inadequate or misleading. For this reason, we have grouped the following signs or symptoms into the same categories, unless otherwise specified: sore throat, dysphagia, odynophagia; dyspnea and tachypnea (grouped as ''tachypnea''); muscle and joint pain; and nausea and vomiting.

More detailed clinical evaluations were done for some patients outside of the quarantine pavilion. As soon as patients were obviously in their recovery phase, they were directed to a nearby ''convalescence'' pavilion, where the risk of contamination was much lower and better records could be obtained.

Four Italian nuns were treated, using extensive precautions, in a private facility adjoining their convent. Two other Italian nuns had been hospitalized early in the outbreak in Mosango, DCR [7], in a private hospital where accurate daily records could be kept. Detailed observations on these cases will be presented separately in this issue [8], but their summary data are included in this global analysis.

Case Definition

A total of 116 available clinical records were first screened to match the clinical definition of EHF used in the epidemiologic survey set up on 13 May [4]. A probable case was defined as a person with (1) unexplained fever and contact with another probable case-patient, (2) unexplained fever plus $\geqslant 3$ of 10 symptoms (abdominal pain, anorexia, asthenia, simple [nonbloody] diarrhea, dysphagia, dyspnea, headache, hiccups, myalgia and arthralgias, and nausea and vomiting), or (3) unexplained acute hemorrhagic signs or symptoms, such as melena, hematemesis, petechiae, or epistaxis.

With the availability of the final laboratory results, the case definition for EHF was revised as follows: (1) Individuals with negative laboratory results who otherwise met the field case definition were excluded, and (2) acutely ill persons for whom clinical information was insufficient to meet the field case definition but who otherwise had laboratory data confirming an acute or recent EBO virus infection (i.e., presence of detectable antigen or IgM antibodies) were included as case-patients. Nine patients were excluded because of insufficient data (8) or duplicate files (1). Four patients who did not meet the case definition were also excluded. Most (97) of the remaining 103 cases that were retained for further analysis fulfilled the first two criteria of the case definition (i.e., they had had contact with a suspected patient and presented with compatible symptoms). In 6 cases, no infectious contact was recorded; nevertheless, they were included in the analysis. In 2 of these cases, previous or concurrent hospitalization for unrelated diseases made nosocomial transmission plausible.

Demographic Data and Global Analysis

The 103 cases analyzed here represent almost one-third of the total number of EHF cases (316 patients) recorded in the global epidemiologic survey of the outbreak in Bandundu region [4] (this issue). In this series, disease onset occurred between 14 April and 21 June, and patients entered the hospital (or their private quarantine area) between 20 April and 24 June. The patients' ages were between 1 and 70 years (mean and median, 38). The sex ratio was 55 females to 48 males.

Eighty-six patients died after a mean of 10.1 days (range, 3–21) after disease onset. The 19 survivors had a mean age of 31 years (range, 12–50 years); 13 were female and 6 were male.

The incubation period could be determined with precision for only 5 patients, all of whom were health care workers (2 died and 3 survived). These 5 patients had had direct contact with patients (no needlestick incidents) during a maximum of 1 day; they became ill a mean of 6.2 days (range, 5–8) after the contact.

The diagnosis of EHF was confirmed by serologic analysis for all patients ($n = 63$) for whom at least 1 serum sample was available (most of the patients had several sequential samples

Table 1. Frequency (%) of symptoms and signs recorded among 103 patients hospitalized during the 1995 outbreak of Ebola hemorrhagic fever in the Democratic Republic of the Congo.

	Patients who died (n = 84)	Patients who survived (n = 19)	P*
Symptoms			
Asthenia	85	95	
Diarrhea	86	84	
Nausea and vomiting	73	68	
Abdominal pain	62	68	
Headaches	52	74	
Sore throat, odynophagia, or dysphagia	56	58	
Arthralgia or myalgia	50	79	.022
Anorexia	43	47	
Lumbar pain	12	26	
Cough	7	26	.028
Chest pain	10	5	
Hearing loss	5	11	
Tinnitus	1	11	
Dysesthesia	0	5	
Signs (nonbleeding)			
Fever	93	95	
Conjunctival injection	42	47	
Tachypnea	31	0	.027
Hiccups	17	5	
Rash	14	16	
Anuria	7	0	
Hepatomegalia	2	5	
Splenomegalia	2	5	
Fetal loss	2	5	
Convulsions	2	0	
Bleeding signs			
Gums	15	0	
Hematemesis	13	0	
Melena	8	16	
Hematuria	7	16	
Puncture sites	8	5	
Bloody stools	7	5	
Petechiae	8	0	
Epistaxis	2	0	
Hemoptysis	0	11 (2 cases)	.033
Hematoma	2	0	
Total	42	37	

* Fisher's exact test, two-tailed; value indicated only when $P < .05$.

collected); this represents 61% of the total number of cases analyzed in this series and 100% of the 19 survivors. Serologic methods are described elsewhere in this issue [9].

Symptoms and Signs

The list of symptoms and signs recorded for the group of patients who died and those who survived is shown in table 1. Fever (axillary temperature of >37.5°C) was almost always noted (93% of the cases). As a rule, the pattern of fever was remittent, and there was a marked tendency toward normothermia during the last 2 days before death.

The disease typically progressed in two phases, with a clinical impression of a relative remission of 1 or 2 days. Early symptoms included fever, extreme asthenia, diarrhea, nausea and vomiting, anorexia, abdominal pain, headaches, arthralgia, myalgia, or back pain. Considered together, myalgia and arthralgia were noted more frequently in survivors than in patients who died, but we suspect that the longer observation time for survivors might have introduced a reporting bias. In our clinical experience, the early phase lasted for no longer than 1 week (generally less), after which, late-onset symptoms were superimposed.

Three of the early-onset manifestations appeared more suggestive of EHF: bilateral conjunctival injection, a maculopapular rash, and sore throat with pronounced pain on swallowing (odynophagia). Rash appeared around the end of the first week, beginning on the lateral sides of the trunk, groin, and axillary spaces; after a few hours, it spread to cover the entire body except the face. The rash was obvious on the white skin of 4 of the 6 Italian nuns, but it was seldom identifiable on black-skinned patients. There was no pruritus associated with the rash, and there was no correlation with the dysesthesia mentioned by some patients; however, the rash was sometimes associated with petechia. No enanthema was reported. At this stage of the disease, the patients either moved toward a second phase with complications, leading invariably to death, or they slowly recovered to a stage of convalescence.

Bleeding of the mucosa and puncture sites, anuria, hiccups, and tachypnea were signs that typically led to death in a matter of days. Most of the nonsurvivors died in a stuporous state with shock and tachypnea. Tachypnea was the most significant criteria discriminating fatal and nonfatal outcomes ($P = .0027$), certainly because this sign usually appeared in the hours preceding death. In 3 EHF cases that developed during pregnancy (all in first trimester), fetal loss invariably occurred ~1 week after disease onset. One of the pregnant patients survived.

In this outbreak, bleeding occurred in only 41% of the patients and did not distinguish those who died from those who recovered. Although no clinical laboratory information was available, blood loss in patients never seemed massive except during abortions, during which immediate volume replacement was required. Bleeding signs generally manifested as oozing from the punctured skin, the gums, and the nose. Prolonged bleeding at intravenous puncture sites was sometimes the first clue to the diagnosis of EHF. Overall, the occurrence of visible bleeding signs indicated a poor prognosis, except for melena and bloody stools, which were sometimes noted early in the disease and occurred in survivors and nonsurvivors. Digestive signs and symptoms (diarrhea, nausea and vomiting, abdominal pain) were very frequent in both survivors and fatal cases.

Lung involvement was poorly documented in patients during the outbreak. On the basis of a limited number of lung auscultations and on the absence of epidemiologic evidence for air-

borne transmission of disease [4], we believe that primary lung involvement by EBO virus was infrequent or had no clinical consequences. Auscultation revealed clear lungs in several patients with terminal tachypnea. One had signs of acute heart failure, and her status was more compatible with acute cardiogenic lung edema. Pericarditis might have been the reason for persistent retrosternal pain in some instances, and in 1 case, the presence of pericardial serous fluid was confirmed by postmortem puncture.

The significantly higher frequencies of coughing (odds ratio, 4.64; 95% confidence interval, 1.25–17.31) and hemoptysis among survivors (table 1) might be the consequence of pulmonary edema from more aggressive parenteral treatment given later in the outbreak, when patient care was improved and needlestick hazard had decreased. As a hypothesis, more cases of myocarditis may have been clinically silent in the first weeks of the observations, when patients were relatively dehydrated as a consequence of safety measures. Toward the end of the outbreak, systematic parenteral rehydration might have improved the overall prognosis, but at the same time, it may have uncovered subclinical lung or cardiac involvement. The frequency of cough among all patients (11% overall) was 6.5% before and 21% after 2 June. It should be noted that antigenic EBO virus material was found in lung and myocardial autopsy samples [10]. Major neurologic symptoms were infrequent.

A few (unrecorded no.) patients had episodes of confusion of unknown etiology. Some had convulsions or clinical signs of meningitis. Tinnitus and hearing loss was reported by patients mainly late in the course of the disease or persisted in the recovery phase; however no correlation was found with the different therapeutic agents that were used (quinine was not used after the arrival of the international team). Other neurologic symptoms that were anecdotally observed were sudden bilateral blindness, dysphonia in the absence of other upper-airway signs, and dysesthesias. The latter were often described as an intense, terebrating sensation of burning on the skin of the trunk and extremities. Hiccups were a relatively frequent (15% of all cases) and intriguing sign, which often seemed to herald a fatal outcome.

Convalescent Manifestations among Survivors

Survivors started to recover ~2 weeks after onset of disease. They slowly regained appetite but remained markedly asthenic, and weight loss was striking. Most of them presented with a number of late complications. They most frequently complained of asymmetrical and sometimes migratory arthralgias, which principally involved the large joints. Other late unexplained symptoms in survivors during 6 weeks of observation are listed in table 2.

Table 2. Late manifestations of Ebola hemorrhagic fever among 19 survivors in the Democratic Republic of the Congo, 1995.

Sign or symptom	No. of cases
Arthralgia	7
Ocular disease (3 patients)	
Conjunctivitis	2
Unilateral loss of vision	1
Uveitis	1
Suppurative parotitis	1
Unilateral orchitis	1
Hearing loss or tinnitus	2
Pericarditis (clinically suspected)	1

NOTE. Survivors were observed for a minimum of 2 weeks and a maximum of 2 months after hospitalization.

Discussion

Overall, the case presentation of EHF in DRC in 1995 was quite similar to that observed in cases in DRC in 1976 [3, 11, 12] and 1977 [13] and in Sudan in 1976 [14] and 1979 [15], and the presentation was similar to that for cases of Marburg virus disease [16, 17] (figure 1).

The frequency of some signs and symptoms of EHF, mainly the hemorrhagic signs, were different than those in previous reports of large series [3, 14]. There are eight explanations that should be considered for these differences: (1) Hospitalized patients might represent a bias toward more severe symptoms or toward patients infected with a virus strain subset that had established its ecologic niche in Bandundu region. However, a retrospective household survey in the region [4] found a comparable frequency of symptoms. (2) Reporting bias may have occurred in previous studies because of retrospective observations. Contrary to information in our series, most of the 1976 information in Yambuku was collected from family members [3]. (3) Some signs, such as exanthema or pharyngeal lesions, were difficult to observe accurately in the poorly lit quarantine wards of Kikwit General Hospital. (4) There may have been differences in the virulence of strains between outbreaks or during different generations of a given outbreak, as suggested previously [3, 11, 15], although limited analysis of virus strains isolated at different times during the 1995 epidemic shows no variations [18]. (5) Different routes of inoculation may have contributed to differences in disease transmission. Notably, the Yambuku outbreak was amplified by the reuse of needles among patients [3], a practice that was prohibited in Kikwit General Hospital; however, as previously stated, needlestick accidents were possible and indeed occurred. (6) Different practices were used in the management of patients (e.g., rehydration and administration of antibiotics) and resulted in various side effects. (7) Prevailing endemic cofactors (e.g., nutrition and infections) may have contributed to differences between the outbreaks. Eight hundred coded sera from the general population during the Kikwit outbreak were screened for human immunodeficiency virus (HIV) infection, revealing a 2.9% antibody seroprevalence. A subset of the EBO patients had negative HIV serology (Swanepoel R, personal communication); therefore, we do not think that the AIDS pandemic

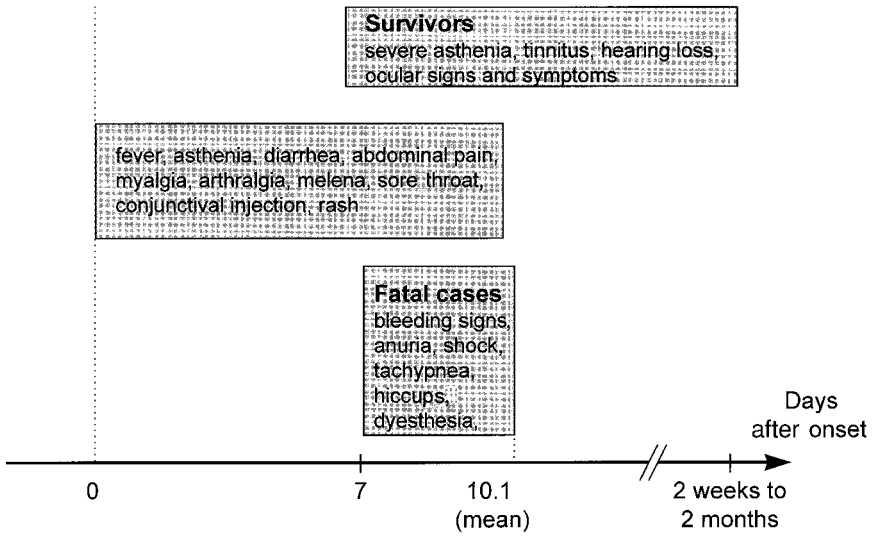

Figure 1. Schematic evolution of Ebola hemorrhagic fever during the 1995 outbreak in Kikwit, Democratic Republic of the Congo.

influenced the clinical presentation or the severity of EHF cases in 1995. Certainly, patients in Kikwit received better hospital care than patients at hospital facilities in Yambuku before they were closed. (8) Cultural and linguistic factors may have influenced the reporting of symptoms, especially in the retrospective collection of data.

The isolates from the 1976 and 1995 outbreaks of EBO virus are virtually identical [1], and the patients' symptoms were grossly comparable, as were the mortality ratios for the two outbreaks. A notable exception is the higher frequency of bleeding signs in the 1976 outbreak, in which 78% of the patients reported some hemorrhagic manifestation. However, in that outbreak, large discrepancies were noted between the retrospective data for deceased patients and the small subset of serologically confirmed cases [3], which may represent a majority of survivors. In Yambuku, 18% of the 34 survivors had hemorrhagic manifestations versus 37% of the 19 survivors in Kikwit. On the basis of immunologic reactivity [19], nucleotide sequence [1], and virulence in nonhuman primates [19, 20], the Sudan strain of EBO (EBO-S) virus is clearly different from those isolated in DRC. The 53% EHF mortality reported in Sudan in 1976 was substantially lower, and some symptoms reported there were more frequent than those in DRC in 1995 (i.e., coughing, chest pain, neck stiffness, psychotic symptoms, and bleeding) [14].

The average incubation period for EHF was 6.2 days, as determined from instances ($n = 5$) of single, well-identified contacts in the 1995 outbreak. Of note, the estimates made in DRC in 1976 [3] and with Marburg disease [16] were quite similar. In Yambuku, as expected, the incubation period for person-to-person transmission of EBO was longer than the incubation period for injections or needlestick accidents [21]. Thus, the empirical recommendation of 3 weeks for quarantine surveillance of EHF contacts [22] appears to be appropriate.

The phenomenon of remitting fever during the terminal phase of disease was previously noted in Marburg hemorrhagic fever [17], in 1 case of EHF in 1976 [12], and in animal models of EHF [20, 23, 24]. In Kikwit, most of the few fatal cases ($n = 6$) who were afebrile during hospitalization died within 2 days with an otherwise obvious presentation of EHF; thus, these patients probably were already in a terminal normothermic phase upon admission.

Early, nonspecific symptoms of EHF are often indistinguishable from those of diseases that are much more common in the tropics, notably malaria, shigellosis, and typhoid fever, and initial management should include empiric therapy against their agents. A maculopapular rash is a classic sign of filovirus infection [11, 12, 25], but it is not always present and notoriously difficult to observe on black skin, as noted in our series and as previously reported [26]. Bilateral conjunctival injection and sore throat/odynophagia are seen in half of the EHF patients.

Hiccups were reported as a symptom in the 1976 DRC outbreak [11, 26]. The mechanism is difficult to establish, considering the multitude of causes [27, 28]. Possible explanations in the context of filovirus hemorrhagic fever include pharyngeal or esophageal irritation, phrenic neuritis, gastric distention by blood, pericarditis, pancreatitis [11, 17], metabolic disorders, or a combination of some or all of these conditions. The postinfluenza encephalitis outbreaks in the 1920s [28] are the other circumstances in which hiccups were noted in epidemic proportions, but there is no definitive clinical evidence that encephalitis was a frequent complication of filovirus infection in Kikwit. Central nervous system involvement may have been more frequent with EBO-S [29] and Marburg virus [30] infections. In the latter case, diffuse panencephalitis with edema has been documented [31]. The abdominal pain, nausea, and vomiting certainly have multifactorial origins. Pancreatitis was suggested

in early outbreaks [3, 26], and digestive mucosal infection occurred and was confirmed by immunohistochemistry techniques in a nonhuman primate model [32].

The physiopathology of human EHF is largely unknown because of the limited number of cases being managed in a medical setting equipped for both safe and exhaustive clinical laboratory evaluations.

Reports of filovirus hemorrhagic fever with extensive laboratory testing concern mainly Marburg virus disease [16, 17]. In 1 case of EHF outside Africa [25], minimal hematologic analysis was delayed for safety reasons, and interpretation of the results was confounded by treatment with interferon. The pathogenesis of bleeding induced by filovirus infection is not well established. Beside thrombocytopenia, disseminated intravascular coagulation (DIC) was indicated in humans by increasing amounts of fibrin degradation products [3, 17], but DIC has not been proven to be the main factor involved in the hemorrhagic diathesis of EHF. In experimentally infected monkeys, there is histologic [20, 33, 34] and late biochemical [35] evidence of DIC, but failure of platelet function precedes thrombocytopenia [35, 36]. From a clinical point of view, some bleeding signs should not necessarily be interpreted as manifestations of an ongoing coagulopathy. Bloody stools alone might simply reflect superinfection of the intestinal mucosa by enteroinvasive pathogens. Similarly, the macroscopic hematuria noted in the survivors might have been related to episodes of concurrent urinary tract infections during their protracted illness.

The high frequency (25%) of hyperventilation as a terminal event was not reported previously. For reasons mentioned above, we believe that this feature reflects underlying metabolic abnormalities rather than cardiac or lung involvement. Metabolic acidosis might be the result of renal impairment, shock, or liver metabolism abnormalities. Some degree of renal tubular necrosis and diffuse, albeit moderate hepatic involvement, have been observed in postmortem samples [10].

It is our clinical impression that hemorrhages and dehydration alone did not account for the terminal shock, although they might have favored hypotension induced by other mechanisms. Adrenal involvement has been shown in monkeys infected by filoviruses [20, 34, 37], but it is not known what role this has in the pathogenesis of the disease in humans. Cardiac failure was frequent in the 1967 European outbreak of Marburg virus disease [30], and clinical suspicion of myocarditis or pericarditis was mentioned by physicians recording active cases of EHF in 1976 in Sudan [14]. Our own observations of at least 2 clinical cases of acute heart failure and 1 case with postmortem evidence of pericarditis add to the suspicion of cardiac involvement being an additional pathogenic mechanism in EHF.

In survivors, recovery is coincident with clearance of the virus from serum (Ksiazek TG, personal communication), but the possibility of persistent replication in specific organs or tissues, with direct local damage or triggering of immune-mediated disease, cannot be excluded as explanations for late-onset manifestations. Orchitis and the ocular clinical manifestations could be, as previously reported, due to the persistence of EBO [25] and Marburg [38, 39] viruses in seminal fluid and in the anterior chamber of the eye [17]. In addition, intercurrent infections, such as malaria or urinary tract infections, were often noted and possibly represent coincidental illnesses. They also may have been late consequences of EHF, with residual immune impairment.

Finally, one of the critical events that permits massive, unrestricted replication of EBO virus in human infection may be an acute immunosuppression induced by the virus itself. This hypothesis is suggested by microscopic examination of liver specimens showing focal necrosis and a striking abundance of viral antigens with minimal or absent inflammatory response [10, 41]; absolute lymphopenia and necrosis of lymphoid tissues in a nonhuman primate model of EHF [20, 33, 35] marked depletion of follicular centers in spleen specimens from fatal cases from Kikwit [10]. Lymphocyte depletion of the spleen and lymph nodes is also a feature of Marburg virus infection in humans [17] and monkeys [41]. Transcriptional editing also produces a secreted version of the EBO virus glycoprotein [1]. Its function is unknown, but by circulating in the serum of patients [1], this protein could divert effectors of the immune response from destroying infected cells.

The assumption of an acute immunosuppression being central to the pathogenesis of EHF implies that clinical management should include the diagnosis and treatment of possible opportunistic infections that might precipitate a fatal outcome. It is tempting to speculate that some of the symptoms reflect superinfection by other pathogens. Also of note in this respect is the unusual case reported by Kalongi et al. in this issue [42]: As a late complication, the case developed an abscess (due to *Mucor* species infection) in the absence of underlying diabetes or neutropenia.

In summary, the above data constitute the first extensive description of the clinical manifestations of EHF recorded prospectively during a large outbreak. They are to be used as the current reference for identification of cases and development of surveillance protocols, and suggest lines of research in the physiopathology of filovirus infection. Additional information on clinical laboratory profiles of EHF patients is urgently needed to manage patients and to direct therapeutic strategies and more detailed clinical investigations.

Acknowledgment

We acknowledge the invaluable collaboration of Médecins sans Frontières Belgium, which provided outstanding expertise and logistic support in restoring the activities of Kikwit General Hospital.

Dedication

This article is dedicated to the health care workers and local Red Cross members in Kikwit who risked their lives to provide

continuing care and to organize rescue before safety measures could be implemented. Many of them contracted EHF and died. A large part of the data analyzed in this article could not have been collected without their commitment.

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