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Full Length Research Paper

Investigation of a haemorrhagic febrile illness in Nakaseke District, Central Uganda: A case series report

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Persons in Nakaseke and neighbouring districts within Central Uganda suffered from a haemorrhagic febrile illness. Four tested positive for the Crimean-Congo Haemorrhagic Fever (CCHF) virus, five for the Rift Valley Fever (RVF) virus, however over twenty tested RT-PCR-negative for Ebola, Marburg, CCHF, RVF and Sosuga viruses. In January-February 2018, we investigated cases and deaths with Viral Haemorrhagic Fever (VHF)-like manifestations that tested negative. Patients isolated at Kiwoko, Nakaseke and Mulago-Kiruddu hospitals were evaluated, homes were visited and hospital records were reviewed, noting admissions with haemorrhage since 2017. The nine isolations had fever and came from Nakaseke and Luweero districts. There was haematemesis, epistaxis, haematochesia, melaena and otorrhagia. Clinical findings included lymphadenopathy, splenomegaly and hepatomegaly. Laboratory analysis revealed anaemia, thrombocytopenia, microfilariae in blood, urine and faeces, schistosome ova in urine and faeces and *Leishmania* in blood. Two deceased had had fever, haematemesis and epistaxis. Home-visiting noted termite mound-riddled terrain, domestic use of pond and swamp water and open excretion. The suspicion of VHF was appropriate, however in Africa there are other possible causes of haemorrhagic fever like the multiparasitism demonstrated which included filariasis, schistosomiasis and leishmaniasis. The communities living environment was considered favourable for the vectors and transmission of the parasites.

Key words: Haemorrhagic fever, multiparasitism, filariasis, schistosomiasis, leishmaniasis, Uganda.

INTRODUCTION

From August 2017 to February 2018 people in Nakaseke and the neighbouring districts suffered from a haemorrhagic febrile illness (Wandera, 2018). According to the Ministry of Health (MoH), four patients from Nakaseke, Luweero and Kiboga districts tested positive for the Crimean-Congo Haemorrhagic Fever (CCHF) virus and five patients from Buikwe, Kiboga, Kiruhura, Kyankwanzi and Mityana districts (Figure 1) tested positive for the Rift Valley Fever (RVF) virus. The real-time reverse-transcription Polymerase Chain Reaction (RT-PCR) test performed at the Uganda Virus Research Institute (UVRI) in Entebbe confirmed the CCHF and RVF infections. However, over twenty patients in Nakaseke tested negative for the Ebola, Marburg, CCHF, RVF and Sosuga viruses. Following concern over the deaths and patients with Viral Haemorrhagic Fever (VHF)-like manifestations, who tested negative for haemorrhagic

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fever-causing viruses, an investigation team was sent to Nakaseke district.

Nakaseke was split from Luweero (Figure 1) and both districts, in north-western Buganda sub-region, are mostly high plain (1 060 – 1 220 m above sea level) bordered by low plain (760 – 1 060 m) to the southwest draining River Mayanja, to the northwest draining River Kafu, to the northeast draining River Lugogo and to the east draining River Sezzibwa. The terrain is partly swamp but mostly brown loam supporting lush vegetation and grey sand supporting thorny shrub, short trees and cactus. The population, largely agriculturalist and pastoralist, stands at 61.48 and 219.3 people per square kilometre for Nakaseke and Luweero districts, respectively (City Population, 2019). The large health units are Nakaseke Hospital (120 beds), Kiwoko Hospital (250 beds) and Bombo General Military Hospital (250 beds).

At Mulago-Kiruddu National Referral Hospital (200 beds) in Kampala, patients admitted to the medical wards with frank or occult bleeding and at times fever had been recognised. They were often referred due to shortage of blood for transfusion at the peripheral health units and for investigation of unexplained anaemias. In 2016 there were 556 such discharged and ran-away patients 195 (35%) having presented with haemorrhage and 153 deaths 57 (37%) having presented with haemorrhage. In 2017, of the 818 discharged and ran-away patients 285 (35%) had haemorrhage and of the 208 deaths 80 (38%) had haemorrhage. In 2018 there were 604 discharged and ran-away patients 248 (41%) of whom had haemorrhage and 145 deaths 68 (47%) of whom had haemorrhage. The bleeding, in order of occurrence, was from multiple sites (also including the respiratory tract, skin, mouth and eyes), then upper gastrointestinal, nasal, rectal, vaginal and urinary. Patients often came from the districts of Kampala, Wakiso, Mubende, Mukono, Mityana, Luweero, Mpigi and Buikwe, Nakaseke district ranked fourteenth. The top referring health units were Mubende Regional Referral Hospital, Mityana Hospital, Kisenyi Health Centre IV in Kampala, Bombo General Military Hospital (GMH) in Luweero, Kiwoko Hospital in Nakaseke, Kitebi Health Centre III in Kampala and St Francis Hospital Naggalama in Mukono, Nakaseke Hospital ranked thirtieth. In this article we present and discuss the clinical and laboratory findings in the patients that were isolated, on suspicion of VHF, at Kiwoko and Nakaseke Hospitals and some aspects of their living environment.

METHODS

From 20th to 30th January 2018 a clinician from Makerere University College of Health Sciences and a veterinary doctor, social scientist and epidemiologist from the MoH were sent to Nakaseke district. Their investigation started at Mulago-Kiruddu National Referral Hospital in Kampala where a suspected patient had tested VHF-negative by RT-PCR done at the UVRI. At Kiwoko Hospital in Nakaseke, patients released from the Isolation Unit to the General Ward were evaluated and at Nakaseke Hospital patients in the Isolation Unit were co-managed. Clinical assessment used physical examination and routine laboratory tests available at the respective health units. Tests included a haemogram, a rapid diagnostic test for malaria, HIV-1 and HIV-2 serology, hepatitis B and C serology and a *Treponema pallidum* haemagglutination test for syphilis. Blood chemistry for liver and kidney function, parasite-specific serology as well as procedures like ultrasonography and endoscopy could not be done. Nonetheless, methanol-fixed Giemsa-stained peripheral blood smears, sedimented and centrifuged urine and wet faecal mounts were examined by light microscopy (WHO, 1991). These specimens were not cultured for bacteriae or evaluated for fungal infection. The homes of the inpatients, those discharged and some deceased were also visited, noting the terrain and vegetation, sources of water for domestic use, excreta disposal practices and the presence of domestic animals.

The individuals were then recorded as the cases, the individuals followed-up and the deceased. A case was a patient with unprovoked bleeding and fever (axillary temperature ≥37.5°C), who had been released from the Isolation Unit to the General Ward after testing VHF-negative; a followed-up individual was a person visited at home who had been isolated with bleeding and fever but tested VHF-negative; a deceased was a hospital-recorded VHF-negative dead who had had bleeding and fever. In addition, the files of patients admitted to the medical wards at Kiwoko Hospital from August 2017 to January 2018 and at Nakaseke Hospital from January 2017 to January 2018 were reviewed, noting admissions due to haemorrhage. Record-review excluded paediatric, maternity, abortion and surgical cases. The records of those individuals who had also been admitted at Mulago-Kiruddu National Referral Hospital were retrieved. Finally, ticks and blood from cattle and goats in the residence of a CCHF-positive case were sent to the UVRI for PCR analysis.

Clearance and ethical consideration

The MoH's National Task Force on Epidemics and Disease Surveillance authorised this investigation in parallel with the emergency response to the three CCHF-positive cases that had been reported in Nakaseke District. Patients, parents or guardians gave written consent on hospitalisation while those followed-up and the parents of the deceased gave verbal consent. The results with respect to privacy would be reported to the

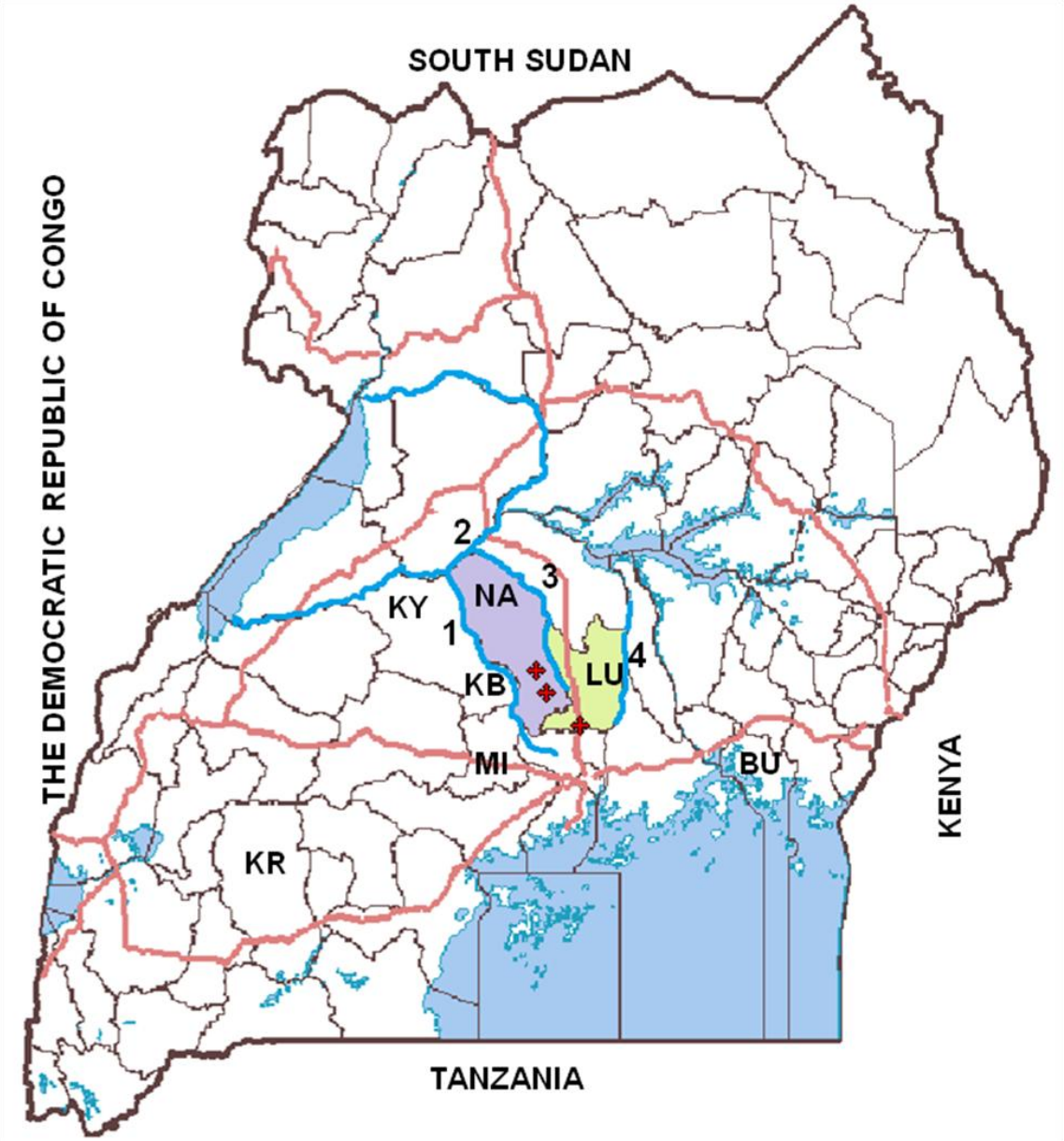

Figure 1. A map showing the districts where CCHF- and RVF-positive cases were reported, the area investigated and the health units. **Districts**: **NA**=Nakaseke and **LU**=Luweero, **BU**=Buikwe, **KI**=Kiboga, **KR**=Kiruhura, **KY**=Kyankwanzi, **MI**=Mityana; **Rivers**: **1**= Mayanja, **2**= Kafu, **3**= Lugogo, **4**= Sezzibwa; **Health units**: ✚=Nakaseke Hospital, Kiwoko Hospital and Bombo General Military Hospital.

health authorities and disseminated at technical and scientific sessions.

RESULTS

Of the 9 individuals investigated, 6 were residents of Nakaseke and 3 of Luweero districts. The ages ranged from 7 to 47 years, 4 patients were aged between 18 and 19 years. The 5 cases found in hospital were male, 3 of them were aged between 18 and 19 years and one died. There was no report of secondarily affected family member, caretaker or hospital staff. Microfilariae were found in blood, urine and faeces. Peripheral blood smears had microfilariae, some unsheathed and some extremely long and knotted at certain points. Figure 2 in parts A to F shows a long microfilarium and the background has a shorter one. In freshly passed urine the cephalic end of a long microfilarium would display a slow rotating snake-like movement punctuated with pauses. For comparison purposes, sheathed *Wuchereria*

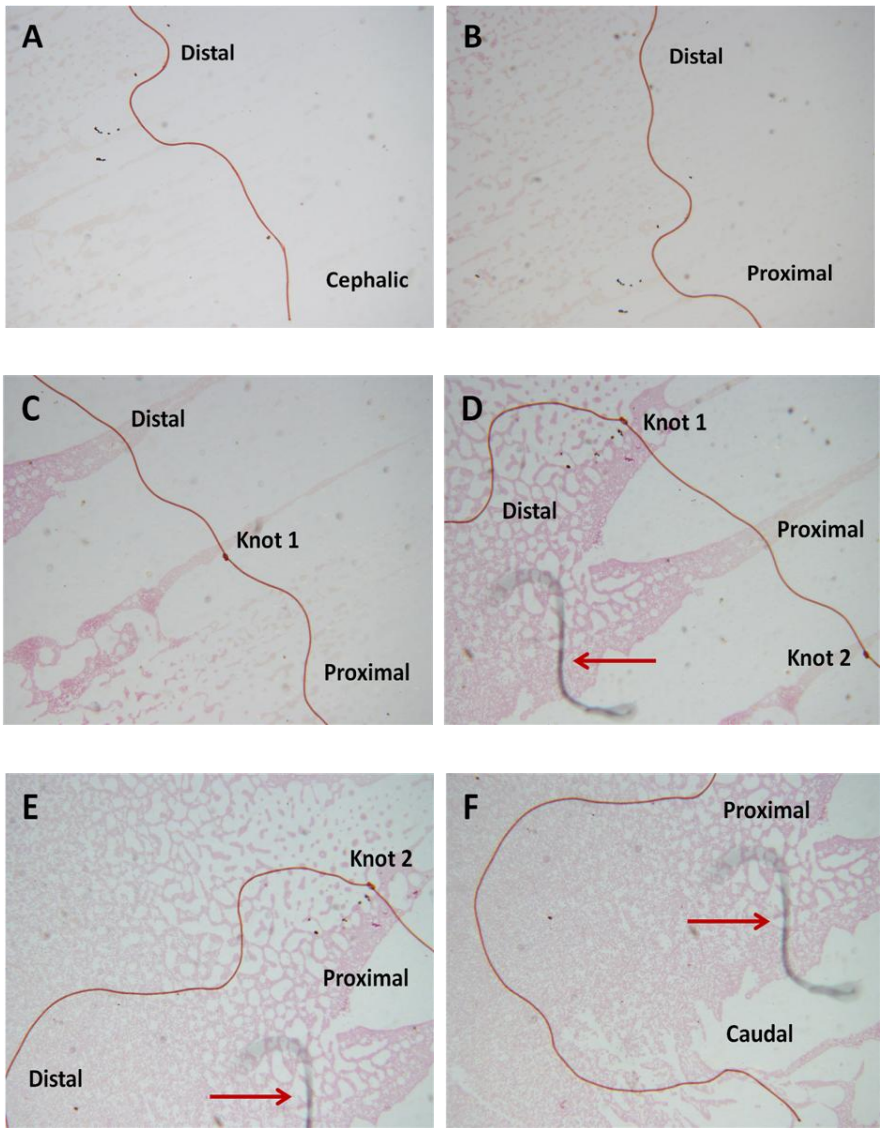

Figure 2. A peripheral blood smear showing in **A** to **F** a long microfilarium with knots, arrowed in the background **D** to **F** is a shorter microfilarium (X 10).

bancrofti measures 250 to 300 mμ x 7.5 to 10 mμ and unsheathed *Mansonella perstans* and *M. ozzardi* 190 to 200 mμ x 4 to 5 mμ and 163 to 203 mμ x 3 to 5 mμ, respectively. The sheathed *Brugia malayi* and *B. timori* measure 177 to 230 mμ x 5 to 6 mμ and 265 to 323 mμ x 4.4 to 6.8 mμ, respectively (WHO, 1997). Also in peripheral blood were Leishman-Donovan bodies clustered within phagocytic cells and some in extracellular space (Figure 3). In urine, fusiform refractile structures 60 x 20 µm, believed to be schistosome ova not typically *Schistosoma haematobium* or *S. intercalatum*, were seen often adherent to squamous epithelial cells and at times to microfilariae (Figure 4 A and B). These structures could as well be found in faeces. Also in faeces were spherical ova similar to *S. japonicum* and *S. mekongi*, circa 120 µm in diameter (Figure 5 A and B) and *S. mansoni* ova 150 x 60 µm (Figure 6). Below we recount the individuals investigated, all were seronegative for malaria, HIV-1 and HIV-2, syphilis and hepatitis B and C viruses and their haemogram results are shown in Table 1. The ticks and blood taken from livestock tested PCR-negative for VHF-causing viruses.

Case 1: **SS** a 47-year-old Muganda farmer from Nyimbwa village in Luweero district was isolated on suspicion of VHF at Mulago-Kiruddu Hospital on 17th

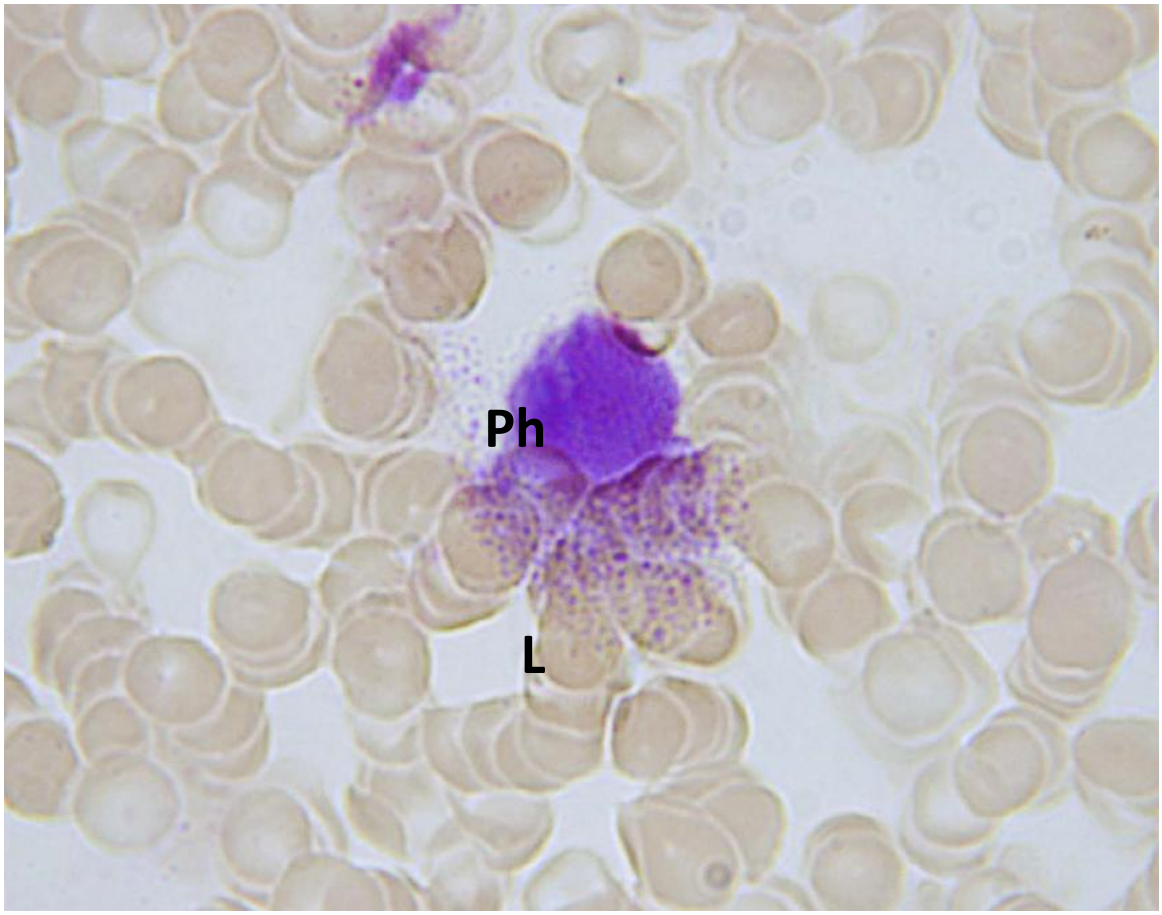

Figure 3. A peripheral blood smear with intracellular Leishman-Donovan bodies (X 100). **Ph**=nucleus of a phagocytic cell, **L**=leishmaniae clustered within a phagocytic cell.

January 2018 having been referred by Bombo GMH in Luweero. He had a week's history of fever, haematochesia and haematemesis and had been transfused due to severe anaemia. He tested VHF-negative and ran away on 19th January 2018 after release to the Gastrointestinal Ward, only a haemogram had been done.

Case 2: **BD** a 35-year-old Rwandese cattle keeper from Wabusaana village in Nakaseke district was released from isolation at Kiwoko Hospital and referred back to Mulago-Kiruddu Hospital after testing VHF-negative. He had been admitted on 16th January 2018, while returning from Mulago-Kiruddu Hospital's cardiology ward where he had been hospitalised in June, September and December 2017. He had fever, cough, haematemesis and oliguria. Physical evaluation noted bronchospasms, mucosal pallor and lower limb oedema, a firm irregular hepatomegaly of 15 cm and splenomegaly of 8 cm. On microscopy, his urine had microfilariae, schistosome ova and calcium oxalate crystals; faeces had microfilariae and *S. mansoni* ova and blood had microfilariae and *Leishmania*. He was subsequently readmitted on Mulago-Kiruddu Hospital's Haematology, Gastrointestinal and Cardiology Wards in January, April and May 2018, respectively.

Case 3: **SD** an 18-year-old Muganda originating from Nansana in Wakiso district worked on a forest plantation in Kyaluweesi village of Nakaseke district. He was isolated at Kiwoko Hospital from 25th to 30th January 2018 with fever and epistaxis. There were microfilariae in his urine, spherical schistosome ova in faeces and microfilariae as well as *Leishmania* in his blood.

Case 4: **TA** an 18-year-old Munyankole high school student from Kyambogo village in Nakaseke district was also isolated at Kiwoko Hospital from 25th to 30th January 2018. He came from a pastoralist community, had been diagnosed with peptic ulcer disease in November 2017 and transfused due to severe anaemia. He presented with fever, abdominal pain, melaena, haematochesia and severe anaemia. Physical evaluation revealed axillary and inguinal lymphadenopathy. He had microfilariae in

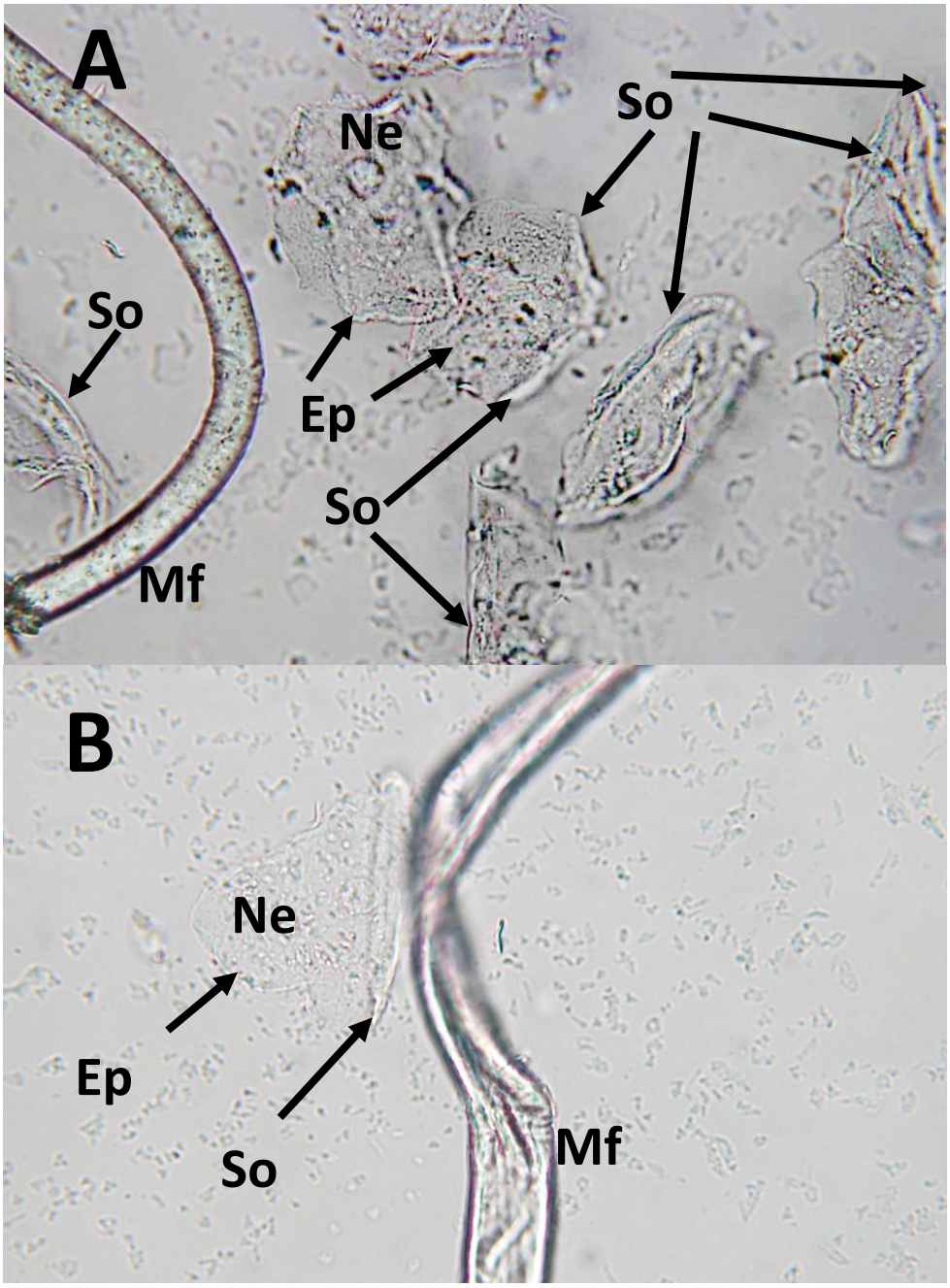

Figure 4. A: Urine sediment with a microfilarium, fusiform schistosome ova with terminal spikes are adherent to squamous epithelial cells; B: A fusiform schistosome ovum is adhered to a squamous epithelial cell and a microfilarium (X60). Mf=microfilarium, Ep=epithelial cell, Ne=nucleus of epithelial cell, So=schistosome ovum.

urine, *S. mansoni* ova in faeces and microfilariae as well as *Leishmania* in blood.

Case 5: **KR** a 19-year-old Rwandese farmer from Lusanja village in Luweero district was isolated at Nakaseke Hospital on 19th February 2018, died on 20th before his VHF test results were known and was buried under hospital supervision. He had a month's history of fever, epistaxis and haematemesis. Clinical evaluation noted a temperature of 40°C, tinge of jaundice, epistaxis, otorrhagia, regurgitation of fresh and altered blood,

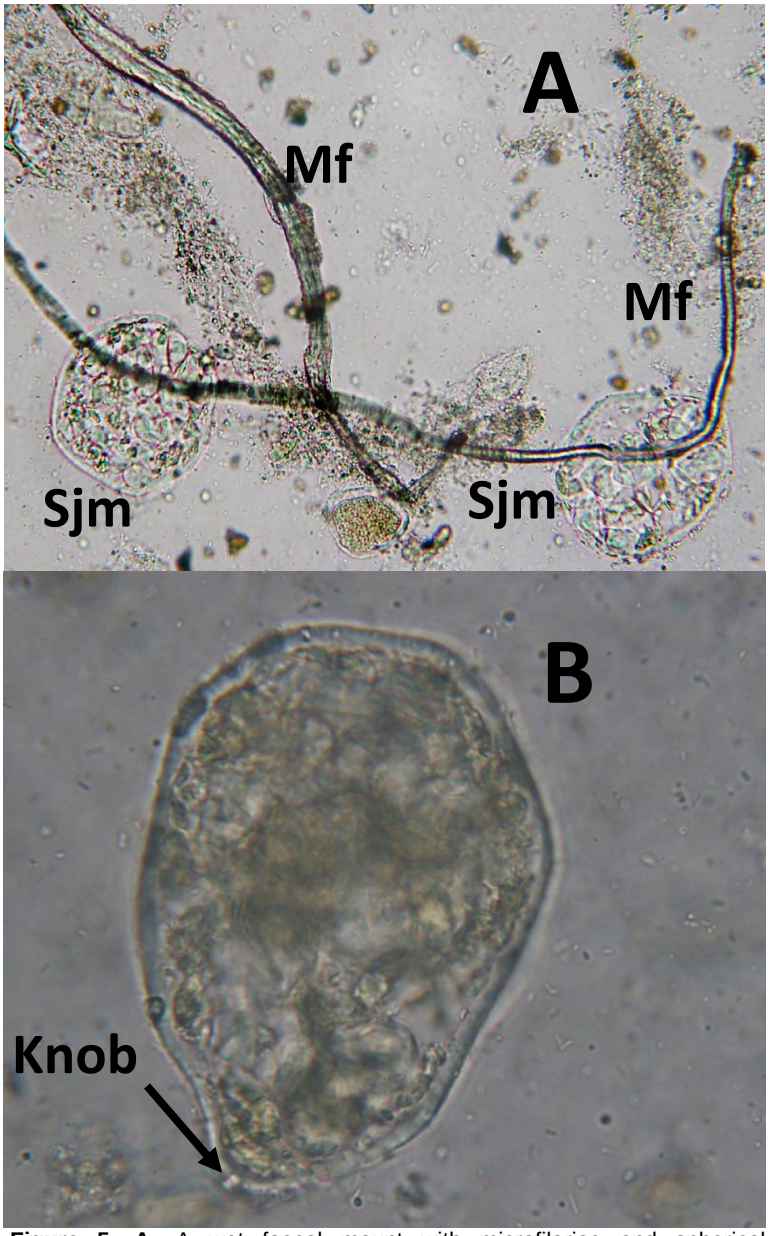

Figure 5. A: A wet faecal mount with microfilariae and spherical schistosome ova. **B:** A knobbed spherical schistosome ovum (X40). **Mf**=microfilarium, **Sjm**=schistosome ova.

haematochesia, axillary and inguinal lymphadenopathy and a splenomegaly of 12 cm. There were microfilariae and *Leishmania* in his blood; he could provide neither urine nor faeces.

Follow-up 1: **NW** a 35-year-old Munyankole cattle keeper from Kalagala village in Nakaseke district was visited at home. He was first admitted at Kiwoko Hospital in August 2017 with haematemesis and severe anaemia. He was then referred to Mulago-Kiruddu Hospital where he was noted with fever, haematochesia, facial and lower limb oedema, a splenomegaly of 30 cm and diagnosed with hypermalarial splenomegaly syndrome. In December 2017 he was readmitted at Kiwoko Hospital with fever, haematemesis, haematochesia and was suspected but he tested VHF-negative. A pancytopenia was then noted and referral made to Mulago-Kiruddu Hospital on suspicion of a haematological malignancy. He resorted to traditional medicine and sought treatment in Rwanda.

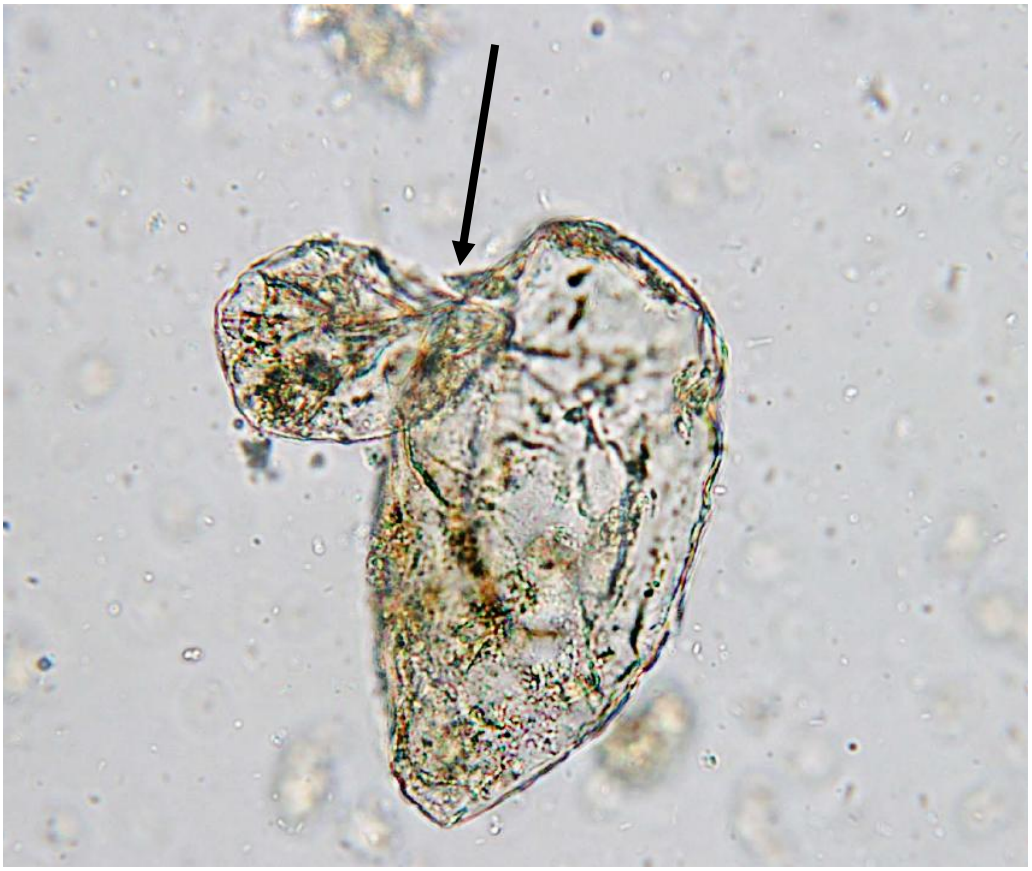

Figure 8. A wet faecal mount with *S. mansoni* ovum, arrowed is the lateral spike (X60).

When visited in January 2018 he was wasted, anaemic and had a splenomegaly of 25 cm. Microscopy revealed microfilariae in urine and blood, schistosome ova in urine, *Dipylidium caninum* ova in faeces and *Leishmania* in blood.

Follow-up 2: **NE** a seven-year-old Muganda primary school student from Kasiiso village in Nakaseke district, whose parents practised mixed farming, had developed fever, abdominal pain and vomiting while her nine-year-old brother, who had tested CCHF-positive, was hospitalised at Kiwoko Hospital in December 2017. NE had had no bleeding and when visited in January 2018 she was healthy but had microfilariae and schistosome ova in urine as well as *Leishmania* in blood.

Deceased 1: **MD** a 19-year-old Muganda secondary school student from an agricultural family in Luvumu village of Nakaseke district was isolated at Nakaseke Hospital on 17th, died 26th July 2017 and had a hospital-supervised burial. He had presented with fever, haematemesis, melaena and erythematous skin eruptions.

Deceased 2: **NB** a nine-year-old Muganda primary school student from Kagugo village in Luweero district who had visited Buswagiro village in Nakaseke district died at her aunt's home but had a hospital-supervised burial. Her aunt, mother and grandmother reported that on 13th January 2018 she had developed fever, epistaxis, haematemesis and convulsions.

Review of hospital records: At Kiwoko hospital 19 males and 17 females had been admitted with haemorrhage from August 2017 to January 2018, six of them had been suspected but they tested VHF-negative. At Nakaseke hospital 22 males and 18 females had been admitted with haemorrhage from January 2017 to January 2018, 12 of them had been suspected but they tested VHF-negative. Overall the patients from Nakaseke district formed 51% (39) and those from Luweero district 38% (29); the 11% (8) came from Nakasongola, Kyankwanzi, Buikwe, Masindi and Kalangala districts. Their age-groups are shown in Table 2 and the bleeding tendencies in Table 3. The haemogram results, where

Table 1. Haemogram results of some VHF-negative patients who were isolated at Kiwoko, Nakaseke and Mulago-Kiruddu Hospitals.

Pt	WBC	Lympho	Mono	Eo	Platelet	Hb	MCHC	MCV
Normal	3-15	1-3.7	0-0.7	0-0.4	150-400	12-18	32-37	86-110
	(x 10^3/µL)					(g/dL)	(fL)	
SS	ǂ2.2	1.3	0.5	13	50	ǁ3.6	22	70
BD	*2.96	1.01	0.45		79	ǁ7	34	63
	ǂ3.95	1.49	0.36	0.26	99	ǁ7	27.6	63.2
SD	*3.29	1.67	0.49		178	14.6	36.1	86
TA	*3.96	0.87	0.32		165	ǁ6.2	37.6	65
NW	ǂ2.24	0.37	0.2	0.1	5	3.1	26.1	80.4
	*1.87	0.26	0.48		37	ǁ4.5	35.9	65
NE	*3.16	1.43	0.62		209	12.4	34.9	83
MD	†1	0.22	0.1		26	11.8	36.1	74

Pt=patient initials, *Kiwoko and †Nakaseke Hospitals reported a collective granulocyte count, ǂMulago-Kiruddu Hospital, ǁ Post-transfusion.

Table 2. Age groups for the patients admitted with haemorrhage to the general wards at Kiwoko and Nakaseke hospitals.

Age group (years)	**Kiwoko** Aug 2017-Jan 2018	**Nakaseke** Jan 2017-Jan 2018	**Totals N = 76**
<10	3	0	3
11-19	5	8	13
20-29	5	9	14
30-39	9	6	15
40-49	5	7	12
50-59	3	2	5
60-80	6	8	14

Data excluded VHF-positive cases.

found, revealed anaemia, thrombocytopenia and at times pancytopenia. Blood chemistry was hardly done and only one result at Nakaseke Hospital mentioned a microfilaraemia.

Home and environment observations: The individuals resided in villages very far apart. The pastoralist communities lived on semi-arid land and excreted in the bushes. They and their herds of tick-infested cattle used water from excavated ponds filled by rain or by swamp water brought in water tanks during the dry season; borehole water was described as caustic and unpalatable. The agriculturalist communities built pit latrines which were prone to collapse and used spring, borehole and swamp water. Expanses of grazing and uninhabited land were covered by termite mounds.

DISCUSSION

This was the first investigation of the alternative causes of a haemorrhagic febrile illness which did not

Table 3. Sites of haemorrhage in the patients admitted to the general wards at Kiwoko and Nakaseke hospitals.

Site of haemorrhage	**Frequency**	
	Kiwoko Aug 2017-Jan 2018	**Nakaseke** Jan 2017-Jan 2018
Vomiting frank or altered blood (haematemesis)	15	12
Bleeding from the nose (epistaxis)	7	8
Passing black stools (melaena)	6	5
Bleeding from the rectum or anus (haematochesia)	4	4
Urinating blood (haematuria)	4	4
Coughing blood (haemoptysis)	4	4
Heavy/prolonged vaginal bleeding (menorrhagia)	4	4
Bloody diarrhoea (dysentery)	1	5
Bleeding from the urethra (urethrorrhagia)	1	1
Bleeding from intestine, skin, eyes, mouth, pharynx (multiple haemorrhage)	1	0
Bleeding from the gums (gingival haemorrhage)	0	1

Data excluded VHF-positive cases.

conform to viral disease due to Ebola (EVD), Marburg (MVD), CCHF or RVF that was being reported by health units in different parts of Uganda. One acknowledged the initial diagnosis of VHF, given the 2018 and ongoing EVD epidemic in neighbouring Democratic Republic of Congo (British Broadcasting Corporation Health, 2019). The subsequent isolation of suspected patients and enforcement of protective personal practices would prevent person-to-person transmission. There was recognition of the other cases with haemorrhage at Kiwoko Hospital, Nakaseke Hospital and at Mulago-Kiruddu National Referral Hospital, as well as the tendency of patients to leave hospital and seek alternative treatment.

The individuals, except the one related to a CCHF-positive case, raised clinical suspicion by manifesting high-grade fever and copious bleeding predominantly from the gastrointestinal and nasal tracts. The haemorrhagic tendency also involved the urinary, respiratory, vaginal, oral and conjunctival mucosae on records-review (Table 3). Previously during VHF incidences, bleeding was more frequent in CCHF and RVF cases (Balinandi et al., 2018; Maurice et al., 2016) than in EVD and MVD cases (Borchert et al., 2011; Mbonye et al., 2012). In other instances, Médecins Sans Frontières (MSF) Swiss while working in north-eastern Uganda recognised epistaxis in patients with visceral leishmaniasis (MoH, 2007; Mueller et al., 2014), an occurrence which was also described in the then Sudan (Siddig et al., 1990) and on the Indian subcontinent (Sigdel et al., 2012). Upper gastrointestinal bleeding was highlighted in adult communities along the Albert Nile in north-western Uganda (Opio et al., 2016) and ashore Lake Albert in western Uganda (Kabwama et al., 2017), where schistosomiasis is endemic. However, the lower intestinal bleeding noted as frank rectal bleeding or haematochesia among the adults presented here had not been documented. On record-review, haematochesia was more frequent than the bloody diarrhoea which was earlier reported in adults with schistosomiasis (Ongom and Bradley, 1972). Even then, gastrointestinal bleeding could also occur in typhoid (De Mel and Wong, 2015), amoebiasis (Dogra et al., 2017) and filariasis (Hajiani and Alavinejad, 2011) which are co-endemic. The fevers were essentially of unknown origin, given the widespread empirical treatment with antimalarials and antibiotics including metronidazole. Nonetheless, fevers were known to accompany filarial, schistosomal and leishmanial infections (Weller and Arnow, 1983; Greer et al., 2018; WHO, 2010). Again on record-review microscopy of blood smears often reported on malarial parasites, urinalysis quoted reagent-strip parameters and microscopy of urine and faeces was hardly done. Although other disease entities were possible causes, the three parasitoses had been recognised at the National Referral Hospital. Patients had been found with microfilaraemia, microfilariuria, microfilaria in faeces and leishmaniae in blood. The schistosome species here described had been found in patients with urinary, peptic and rectal symptoms, haematuria, haematemesis, haematochesia and unremitting fevers. On treatment with praziquantel and ivermectine combined with albendazole and mebendazole some patients improved remarkably, no treatment would be given for the leishmaniasis.

While the enlarged lymph nodes, spleen and liver implied lymphoreticular involvement, the bicytopenia (Table1) and pancytopenia (records-review) could suggest haematopoietic impairment. Secondary lymphoid and mononuclear phagocytic systems (Henry, 1972) can be stimulated by parasites; a reactive hyperplasia, inflammation or granuloma formation may ensue. Filaria and their antigens induce lymphatic endothelial cell proliferation (Bennuru and Nutman, 2009) and pathology; schistosome ova directly injure, induce inflammatory reactions and cause liver and splenic disease (Ongom, 1972; Wilson et al., 2011). The leishmaniae infect circulating and tissue mononuclear phagocytic cells and were associated with bone marrow malfunction in visceral leishmaniasis (WHO, 2010). In multiparasitism, as were the cases we describe, specific disease may be aggravated (Hotez et al., 2008); nonetheless we suppose that the resultant syndrome would depend on the predominating parasite, organs involved and nature of the immune response. On record-review we recognised differential diagnoses of idiopathic thrombocytopenic purpura, bone marrow failure, hyperreactive malarial syndrome and lymphoma, as well as haematological, hepatocellular and abdominal malignancies.

The bleeding febrile individuals prompted suspicion of VHF however, the lack of person-to-person transmission, wide dispersal of cases as well as the non-confirmation of livestock disease even where a person had tested CCHF-positive favoured an alternative cause. Patients with frank and subtle bleeding were well-known at the National Referral Hospital and Luweero ranked sixth and Nakaseke fourteenth among their districts of origin. That the adult age groups were evenly affected, males and females alike, was evident from the records (Table 2) however from this investigation, adults aged less than 20 years were likely to be isolated as VHF suspects. On their infection with schistosomes and filariae, the means of exposures may have been contact with surface water contaminated with human or even animal faeces and urine and bites from day- and night-feeding mosquitoes and midgets. On the other hand, the infection with leishmaniae was less explicable. It was nonetheless noted that in north-eastern Uganda, where visceral leishmaniasis caused by *Leishmania donovani* is endemic, termite mounds were dwelling places for the phlebotomine vectors (MoH, 2007).

We supposed that the exposure of the communities to the parasites was more recent than that known in the endemic areas where MoH's Neglected Tropical Diseases (NTD) control programmes were active (MoH, 2013). Besides Nakaseke, other central districts were implicated by the records at the National Referral Hospital. Indeed, haemorrhagic fever was more conspicuous but only one of the syndromes linked to the multiparasitism. The helminthiases result partly from efficient transmission of parasites by mosquitoes, midgets and molluscs, vectors which thrive in environments with abundant surface water. In the prevailing situation the water may be contaminated with human or animal faeces and urine. For over a decade people have dwelt in environments where flooding is frequent, use of swamp water is popular and sanitation is inadequate. Furthermore, human movement from upcountry, neighbouring South Sudan, Somalia, Ethiopia, Eritrea and the Democratic Republic of Congo (DRC) as well as from distant China, India and Southeast Asia could expose naïve and thus vulnerable communities to new parasite species. By 2010 for instance Leishman-Donovan bodies were demonstrable within phagocytic cells in the blood ingested by *Tunga penetrans*. Histology slides of specimens enucleated from mostly primary school-age children during an outbreak of human tungiasis in the eastern Busoga sub-region were examined by microscopy (unpublished work).

Limitations of the investigation

This investigation was greatly confined by the fear of person-to-person transmission of VHF-causing viruses, the limited health facility resources and the lack of funds to revisit individuals or investigate similar incidences elsewhere in the country. While patients were in isolation physical examination and sample taking and processing even for blood transfusion was complicated. Thus if a patient died or ran away after release from isolation their samples would be lost. The fear of infection remained even after exclusion of VHF, further compromising patient-care. Most importantly, although schistosomes, filariae and leishmaniae were demonstrated in blood, urine and faeces on microscopy, other parasites might have been missed. There was no exclusion of bacterial and fungal infection, organ-function was not evaluated and no endoscopic examination was done. It could therefore not be concluded that the parasites were the sole cause of the haemorrhagic febrile illness. Finally, the inpatients, those followed-up and their household members were given anti-filarial and anti-schistosomal medicines but not revisited. Antihelminthic treatment could reduce the risk of recurrence, prevent disease and the results would inform the national policies governing NTD control.

CONCLUSION

The patients admitted to Nakaseke, Kiwoko and Mulago-Kiruddu hospitals' Isolation Units came from Nakaseke and Luweero districts. They had fever and bled predominantly from the gastrointestinal and nasal tracts. Clinical evaluation revealed lymphoreticular involvement and laboratory investigation suggested haematopoietic

impairment. The initial suspicion of VHF was appropriate given the 2018 and ongoing Ebola outbreak in the DRC, also involving East African countries, and the need to prevent person-to-person transmission. However, we suppose that among the other possible causes of haemorrhagic fever is the multiparasitism that was demonstrated which included filariasis, schistosomiasis and leishmaniasis. The living environment was favourable for the vectors of the parasitoses and the proximity of humans to surface water could facilitate the transmission of the parasites.

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Conflict of interest

The authors declare no conflict of interest.

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