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Alkhumra haemorrhagic fever: case report and infection control details

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A tickborne encephalitis virus of the genus *Flavivirus* was isolated for the first time in Saudi Arabia in 1995.¹ Flaviviruses are single-stranded positive-sense RNA viruses responsible for many serious diseases in humans (e.g., yellow fever and dengue fever). The new isolate, termed Alkhumra virus (ALKV), is one of only three tickborne flaviviruses known to cause haemorrhagic disease in humans; the other two being Kyasanur Forest disease virus and Omsk haemorrhagic fever virus.^{2,3} Alkhumra haemorrhagic fever and ALKV take their name from the Alkhumra region of Makkah province (which includes the holy cities of Makkah, Jeddah, and Tayef). Alkhumra is a largely agricultural area 230 km east of Tayef and about 1000 km west of the capital city, Riyadh (Fig. 1).

In 2001 the complete coding sequence of the prototype strain of ALKV was published;⁴ however, the mode of disease transmission has not been fully described. Limited observation suggests that human ALKV disease may result from contamination of a skin wound with the blood of infected sheep, from infected tick bites, or by drinking unpasteurised contaminated milk.⁵ To date, only 24 symptomatic cases of Alkhumra haemorrhagic fever have been reported, and the mortality rate is 25%.⁵ The disease is

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Table 1. Laboratory results on admission.

	Result (Normal Value)
White cells (per mm ³)	3300 (4-11,000)
Differential count (%)	
Lymphocytes	24 (20-45)
Polymorphs	67 (36-75)
Monocytes	4 (3-9)
Bands	5 (5-11)
Platelets (per mm ³)	19,000 (150-400,000)
Liver profile	
ALT (U/L)	907 (10-40)
AST (U/L)	1003 (15-40)
LDH (U/L)	3564 (100-190)
CPK (U/L)	13,992 (38-174)
Albumin (u/L)	27 (34-48)

Table 2. Appropriate use of personal protective equipment for 17 contacts.

	Sometimes	Always	Never
Mask	2	15	0
Gown	3	14	0
Gloves	0	17	0
Face Shield	0	0	17

rare and presently confined to Saudi Arabia, but it may be of wider interest because of the large number of international travellers who visit the country, especially during the Hajj season when close to 1.5 million pilgrims arrive in the holy cities of Makkah and Al Madina.

The risk of nosocomial transmission of ALKV virus is not known and no published infection control recommendations are available for healthcare workers to follow. Here, the first case of ALKV infection imported from the southern region of Saudi Arabia, and which was diagnosed in Riyadh, is reported. In addition, detailed infection control precautions taken to prevent nosocomial transmission of ALKV are presented.

A 25-year-old single male who worked as a police officer in the Ministry of the Interior in Najran presented to the emergency department at King Abdulaziz Medical City (KAMC) with a four-day history of mild fever and subsequent rapid deterioration in his condition. Najran lies in the south-west of Saudi Arabia (Fig. 1), bordered by Yemen to the south and Oman in the east. The patient's symptoms included fever (38.5°C), chills and decreased level of consciousness. Initially, he was admitted to a Ministry of Health hospital after one day of illness but discharged himself against medical advice two days later. His condition deteriorated and he developed haematemesis and melaena. Four days into his illness he was brought to the emergency department and his symptoms included jaundice, gingival bleeding, flapping tremors and confusion. The emergency staff suspected haemorrhagic fever and the patient was

Fig. 1. Map of Saudi Arabia showing the Alkhumra area in the south-west of the country.



placed in a negative-pressure isolation room and strict contact precautions were exercised with all aspect of patient care.

On examination, the patient was a well-built (weight: 70 kg) young man. His Glasgow Coma Scale rating was 13/15. Generally, he was mildly icteric with obvious bleeding from his gums. No other bleeding sites were noted. There were no skin lesions and the remainder of his examination was normal.

Laboratory test results are shown in Table 1. Urinalysis showed the presence of red blood cells. Serological tests for Rift Valley haemorrhagic fever (RVF), dengue fever, West Nile virus, cytomegalovirus, hepatitis C virus, hepatitis A virus, human immunodeficiency virus, brucella and francisella were all negative. However, serology for ALKV, which was sent to the Saudi Ministry of Health laboratory in Riyadh was positive. A repeat sample was sent to Dr Sulaiman Fakeeh Hospital virology laboratory in Jeddah and was also positive.¹ The Ministry of Health results were available on the day of discharge, while the results from Fakeeh Hospital were only available after four weeks.

During his hospital stay, the patient received supportive care with intravenous fluids. No pressors were needed and the patient was never intubated. Signs of recovery became evident on the fourth day after admission and he had fully recovered by the sixth day and was discharged. The patient was seen on follow-up three months later and was in good condition with no permanent central nervous system impairment.

Two to three weeks later a list was compiled of the healthcare workers who had come in contact with the case. A questionnaire was prepared by the infection control practitioner and distributed to gather information on compliance with infection control policies carried out during the hospitalisation of the patient, as well as to establish the degree of involvement/exposure, use and adherence to isolation procedures, standard precautions, personal protective equipment and hand hygiene practices (Fig. 2.). The results of the questionnaire are shown in Table 2. Household and other contacts were not available for screening. The patient lived with his parents and brother, and none of these family members became ill.

Fig. 2. Questionnaire completed by 17/19 healthcare contacts.

<p>On admission, was the patient placed in isolation? If yes, type of isolation:</p> <p><input type="checkbox"/> Single room</p> <p><input type="checkbox"/> Negative pressure</p> <p><input type="checkbox"/> Positive pressure</p> <p><input type="checkbox"/> Neutral</p> <p><input type="checkbox"/> Anteroom</p>																							
<p>If not isolated, was the patient cohorted with any other patient?</p> <p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>																							
<p>While attending to the patient, do you recall having had direct contact with the patient's:</p> <p><input type="checkbox"/> Blood <input type="checkbox"/> Body fluid</p> <p><input type="checkbox"/> Any cutaneous injury</p>																							
<p>Extent of involvement with patient:</p> <p><input type="checkbox"/> Primary nurse <input type="checkbox"/> Casual contact</p> <p><input type="checkbox"/> Covering <input type="checkbox"/> No contact (on same shift)</p> <p><input type="checkbox"/> Other, please explain</p>																							
<p>Appropriate personal protective equipment usage:</p> <table border="1"> <thead> <tr> <th></th> <th>Sometimes</th> <th>At all times</th> <th>Never</th> </tr> </thead> <tbody> <tr> <td>Mask</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Gown</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Gloves</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Face shield</td> <td></td> <td></td> <td></td> </tr> </tbody> </table>					Sometimes	At all times	Never	Mask				Gown				Gloves				Face shield			
	Sometimes	At all times	Never																				
Mask																							
Gown																							
Gloves																							
Face shield																							
<p>Procedures performed on patient:</p> <p><input type="checkbox"/> IV catheter insertion</p> <p><input type="checkbox"/> Foley catheter insertion</p> <p><input type="checkbox"/> Mouth hygiene</p> <p><input type="checkbox"/> Other, please explain</p>																							
<p>Was proper hand cleansing carried out with patient care?</p> <p><input type="checkbox"/> Yes</p> <p><input type="checkbox"/> No</p>																							

Nineteen healthcare workers (including 17 primary care nurses) had documented contact with the patient. Of these, 17 completed the questionnaire and provided blood samples for antibody testing following verbal consent. Control samples were collected from expatriate healthcare workers who presented at the employee health clinic for blood tests but had no contact with the reported case. All blood samples from contacts and controls tested negative for Alkhumra antibodies.

Compliance with negative-pressure isolation was 100% in the emergency room and on the ward. Upon admission of the patient to the ward, concerns about nosocomial spread of haemorrhagic fever viruses were raised. The

patient remained in isolation for the duration of his hospital stay. Of the healthcare workers who attended the patient, 80% wore masks at all times, while 100% compliance with glove use was documented. Procedures performed on this patient included insertion of a peripheral intravenous catheter and a Foley catheter, and routine mouth hygiene. As none of the procedures carried the risk of aerosolisation and no active haemorrhage was documented, face shields were not used.

In the first report of ALKV infection from Jeddah, the cases documented were either butchers or had direct contact with sheep before becoming ill.¹ This indicated that the disease was likely to be a zoonotic viral infection. However, other modalities of disease transmission have not been excluded. As with other viral haemorrhagic fever disease, where maximum precautions were taken, no secondary cases were identified among the healthcare workers involved.

Najran is located in the southern region of Saudi Arabia, bordering sub-Saharan Africa, and is an area in which haemorrhagic fever is known to be endemic. It is a large agricultural area in which inhabitants are exposed to a wide variety of animals in living accommodation that has few amenities. Rainfall in this area is abundant and consequently the resultant lush vegetation provides a suitable reservoir for agents of haemorrhagic fever.

However, further sero-epidemiological studies are needed to delineate which agents are endemic in which parts of the country, and this would be valuable when managing patients with symptoms of haemorrhagic fever in the future.

Alkhumra virus is a new infectious agent and much remains to be discovered about its transmissibility, including its mode of infection and minimum infectious dose. The strict infection control steps practised during this patient's hospitalisation in KAMC may not have been the main reason for the lack of nosocomial transmission of the disease. For example, the virus may be particularly refractory to person-to-person transmission, as is the case with the avian influenza H5N1 virus responsible for human fatalities in south-east Asia in 2004.

This speculation is supported by the fact that none of the victim's relatives contracted the disease during its period of maximum virulence, despite negligible containment practices either at home or in the first hospital to which the victim was admitted. The patient was not exposed to high-risk procedures (e.g., intubation), which may have aerosolised infectious particles, and there is a lack of historical evidence for person-to-person spread of this particular virus.

Strict compliance with infection control practices for patients with suspected viral haemorrhagic disease is very important, especially in areas where it is known to be endemic. In September 2000, Saudi Arabia suffered its first major outbreak of RVE.⁸ Further spread of the disease was minimised, with the Ministry of Health and National Guard Hospital playing an important part in this regard.

Finally, with the emerging threat of biological warfare, healthcare workers should have a high index of suspicion when dealing with suspected cases of viral haemorrhagic disease. Involvement of the hospital epidemiologist and/or infectious disease specialist is crucial and the institution should identify a clear chain of communication to ensure a multidisciplinary approach. However, for maximum effectiveness, periodic readiness drills should be undertaken.^{9,10} □

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