



Case report

First confirmed case of human rabies in Saudi Arabia

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A B S T R A C T

Rabies is an almost invariably fatal Lyssavirus-induced disease, that causes acute encephalitis in humans and other mammals. The viral reservoirs include both wild and domestic animals. The infection causes about 24000 to 60000 deaths worldwide per year (Giesen et al., 2015; Naghavi et al., 2015) with Africa and Asia having the majority of human deaths (95%) caused by rabies. Rabies is endemic in animals in Arabian peninsula. Some countries in the region such as Saudi Arabia, Yemen and Oman are reporting increasing number of cases of wildlife rabies. Among these countries Saudi Arabia is largest, but published data regarding the rabies status in the country are scarce. We report a case of a 60 year old Saudi man who was admitted to cardiac ICU of a tertiary care hospital in Makkah, primarily with history of chest pain for cardiac evaluation, who was found to have signs suggestive of hydrophobia. On history, it was found that he had an unprovoked scratch on his face by a dog in Morocco a month prior to admission and his saliva PCR test confirmed rabies virus.

Introduction

Rabies is a zoonotic disease caused by Lyssavirus which is endemic in animals in Arabian Peninsula. During the period of 2007–2009 a total of 11069 animal bites to humans have been reported to the Saudi Ministry of Health and Saudi Ministry of Agriculture. Most of bites were related to dogs (49.5%) and cats (26.6%), followed by mice and rats, camels, foxes, monkeys and wolves [3]. Some countries in the region like Saudi Arabia, Yemen, and Oman are reporting increasing number of cases of wildlife rabies [4]. Among these countries, Saudi Arabia is the largest, but published data regarding the rabies status in the country are scarce.

Case report

A 60 year old Saudi man presented to an nearby community hospital in September 2016 with nausea, vomiting and epigastric pain followed by chest tightness. His past medical history was significant for hypertension and type 2 diabetes. An Initial EKG was not consistent with acute coronary syndrome and an upper endoscopy on the same day showed features suggestive of gastritis. During the procedure he developed respiratory distress and tachycardia and was transferred to an intensive care unit. There, he had worsening chest pain and had a brief episode of ventricular tachycardia. The patient was transferred to King Abdullah Medical City (KAMC) in Makkah with diagnosis of acute anteroseptal myocardial infarction for further management where he

underwent a coronary angiogram suggestive of two vessel disease with left main involvement and surgical intervention was planned. Infectious disease was consulted because of leukocytosis and the consultation team found him with severe retching while attempting to drink water. Due to this hydrophobic behaviour, a retrospective re-evaluation of history was done. The patient reported that a month before admission he visited Morocco and sustained a major unprovoked dog scratch to his face that required sutures. He stated that he received only a tetanus vaccine. He denied any fever or headache but there was a history suggestive of one episode of seizures. He was afebrile with no signs of meningeal irritation. He had a small healed linear scar near his right eye measuring around 2–3 cm. The rest of the examination including neurologic examination was unremarkable. He was given rabies vaccine (Verorab 0.5 mL IM one dose each on right and left deltoid), and human hyperimmune rabies immunoglobulin (20 IU/kg) IM.

Investigations revealed mild increase in leukocyte count ($13.33 \times 10^9/L$), serum creatinine (1.53 mg/dL) and AST (77 U/L) levels with significant elevation of troponin I (4.65 ng/mL) and CKMB (30.08 ng/mL). Lumbar puncture was performed and the CSF was sent for rabies PCR. His CSF did not show any white blood cells, whereas there was mild increase in protein (48.8 mg/dL), with glucose being 166 mg/dL (serum glucose–200 mg/dL). His saliva and skin sample were also sent for rabies PCR. On the day after admission, patient developed pulmonary edema and cardiac failure, consequently got intubated and mechanically ventilated. His saliva sample for rabies PCR was reported positive on day 2. In view of establishment of diagnosis

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with saliva PCR, regional laboratory did not process the CSF and skin biopsy sample for rabies PCR for the reason of cost effectiveness. He was started on oral Ribavirin 400 mg (CrCl–32 mL/min) and continued on IV Midazolam maintenance dose of 0.1 mg/kg/hour, which was started as part of sedation for mechanical ventilation. Request was sent to pharmacy to procure Interferon-alfa from other health care facility. On the 3rd hospital day, he had an episode of ventricular tachycardia (VT), which reverted back to sinus rhythm after DC cardioversion and was started on small doses of inotropes for hypotension. Patient care was continued in cardiac ICU, where he had persistent elevation of serum creatinine and cardiac enzymes. The brain images were unremarkable. Ribavirin was put on hold in view of drop in hemoglobin (from 13.8 to 8.8 g/dL), worsening cardiac condition and hemodynamic instability. On the 5th hospital day he had recurrent episodes of VT, progressively worsening hemodynamic parameters and he succumbed to his infection on that day. Look back program was done to follow Health care workers (HCW). Rabies prophylaxis was given to 86 HCWs who were exposed to the patient. They were provided with information of possible signs and symptoms which should alert them for review. So far after 17 months none of them reviewed with possible signs or symptoms of rabies.

Discussion

Every year millions of people from around 184 countries arrive to Makkah and Madina for Umrah and the Hajj pilgrimage. According to official censuses a total of 2,352,122 pilgrims attended Hajj in 2017, which was increased from 1,862,909 in 2016 and 1,952,817 in 2015 [5].

With an increasing young population with easy accessibility to social media, Saudis show more interest in travelling, especially other countries in Arabian Peninsula. Consideration must be given to the potential risk of transfer of infection from other countries in Arabian Peninsula and other neighboring countries (which appears to be the possibility in present case), where rabies is more prevalent [2] than Saudi Arabia, as flow of population within these countries is frequent. The case here had symptoms suggestive of furious rabies, and we believe that it is first confirmed case of human rabies in Saudi Arabia (confirmed by PCR of saliva). He had severe retching while attempting to drink water, possibly due to involuntary pharyngeal muscle spasms. Hydrophobia is most characteristic clinical feature of rabies, seen in 50 to 80 percent of patients [6,7]. After initial feeling of discomfort in the throat or dysphagia, the patient develops an overwhelming and sudden terror of water associated with involuntary pharyngeal muscle spasms during attempts to drink. Later in the disease, even the mention or sight of water may trigger these involuntary spasms.

There is need for a high index of suspicion to consider rabies as possibility despite its rarity in human beings in Saudi Arabia. The absence of an exposure history does not exclude the diagnosis. There is possibility of missed cases of rabies encephalitis, not recognised due to a long incubation period [1] and remote exposure history which majority of times might have not been conveyed to the treating physician due to unawareness of its importance. In case of our patient, the incubation period was about one month.

Even though rabies is endemic in North Africa, exact data on incidence are meagre. Various initiatives are working to provide reliable data on rabies epidemiology, to raise rabies awareness and design programs for rabies control. The annual incidence is seen to vary from 0.02 cases/100,000 people in Tunisia to 0.1 cases/100,000 people in Egypt. These differences may be result of variations in the epidemiologic statistics of animal rabies and the availability of rabies post-exposure prophylaxis (PEP). Rabies PEP availability is subject to large differences; the lowest (0.4 persons receiving rabies PEP/1000 population) have been reported from Sudan, whereas the highest (3.3 persons receiving rabies PEP/1000 population) were reported from Tunisia. In Morocco, a majority (90%) of human rabies cases are due to

dog bites and which are mainly from rural areas. Human deaths from rabies in Algeria occur mostly in northern and coastal part of the nation [8–12] and a majority of cases of animal rabies were reported from dogs, which accounted for > 40% laboratory confirmed rabid animals. There were also reported cases of rabies from sheep, cattle, cats, goats, and horses. Morocco is spread over 446,500 sq. km, sharing its borders with Western Sahara and Algeria. With an estimated population of around 32.5 million (2012), Morocco has about 57% of its population in urban areas. Rabies being endemic in Morocco with all regions affected with the exception of southern desert region. In Morocco, sometimes human rabies cases are laboratory confirmed, whereas majority of times it is diagnosed only on clinical grounds. Since 1986 an average of, 22 human deaths associated with rabies occur yearly [13].

As per CDC recommendations, if someone is traveling to a country with widespread rabies, it is advised to consider pre-exposure vaccination if: (1) Planned activity will bring into contact with wild or domestic animals, for example if the traveller is a biologist, veterinarian, or agriculture specialist working with animals, (2) If person will be visiting remote areas where medical care is difficult to obtain or may be delayed, for example, hiking through remote villages where dogs are common, (3) If persons stay is longer than 1 month in an area where dog rabies is common. The longer one stays, the greater the chance of a rabid encounter with an animal [14].

Conclusion

Although prevalence of human rabies is rare in Saudi Arabia, there is always a potential risk given the multiple factors including, prevalence of rabies among animals, flow of population among other neighboring countries with prevalence of rabies, and millions of pilgrims visiting Saudi Arabia yearly. There is need for establishing travel health centers in Saudi Arabia. These centers will offer counselling, education, pre-travel vaccination and prophylaxis to international travelers. This case also emphasizes need for further strengthening, standardization and universalization of travel guidelines globally.

Conflict of Interest/Funding

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