Original article

Familial cluster of exposure to a confirmed rabid dog in travelers to Algeria

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A B S T R A C T

A 10 person-family originating from Algeria traveled in rural Algeria for the purpose of visiting friends and relatives without seeking pre-travel advice, did not receive pre-travel rabies immunization, and were exposed to a confirmed rabid dog including 8 within less than 4 days of arrival. Three received suckling mouse brain rabies vaccine although WHO strongly recommends that its production and administration be discontinued and seven received insufficient doses of equine rabies immune globulin abroad. Rabies treatment was completed on returning to France. This reports underline the fact that travelers visiting friends and relatives in dog rabies endemic country are at high risk of rabies exposure and unaware of such a risk in most instances. Rabies risk warning should be reinforced and rabies pre-exposure vaccination should be considered in all individuals traveling to North Africa (and to sub-Saharan Africa) whatever the duration of stay.

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On 19th August 2016 a patient presented to Marseille rabies treatment center with a history of exposure to a confirmed rabid dog in Algeria. Anamneses revealed that indeed, ten members of a family, originating from Algeria and living in Marseille, France, including two children of ten and twelve years have been in contact with the rabid dog in Bouzeguene, an Algerian rural village in Kabylie region, where they traveled for holidays and participated to a wedding. On 9th, August 2016, one of the family children found and adopted a free roaming eight month old puppy. The dog was kept at home and fed by the family members. On 17th August 2016, the dog exhibited behavior changes with aggressiveness, hyper-salivation, hydrophobia and anorexia, rapidly followed by a paralysis of the front left leg that generalized in the next hours. The dog deceased on the next day. A local veterinary took off the animals’ head, which was transported to Alger Pasteur Institute by the family. Two days after, the rabies diagnosis had been confirmed in the dog. The five other patients received CCDRV. In Marseille, risk assessment of these eight patients, based on World Health Organization (WHO) criteria [2] was as follows: category 1: 4 patients, category 2 and 3: 2 patients each (Table 1). Category 2 patients received CCDRV completion as well as category 1 patients considering that a full course of vaccine would provide preventive immunization in case of further travel to Algeria. One category 3 patient presented 21 days after the first vaccine was provided abroad at the time the administration of RIG in contra-indicated [3]. In this patient, we only completed his CCDRV course. The remaining category 3 patient presented 3 days after a course of SMBRV was started in Algeria. In this patient we had received preventive pre-travel vaccination against rabies.

Eight patients started a rabies post-exposure prophylaxis (RPEP) in Algeria where they were classified type 3 exposure according to Algerian criteria [1] (Table 1). They received equine rabies immune globulin (ERIG) a few days later except in one patient who leaved for France. However, according to family members, the hospital did not have enough quantity of ERIG; therefore they decided to share available vials, in order that each person received at least one injection. Three patients were initially vaccinated with suckling mouse brain rabies vaccine (SMBRV), two of whom were switched on a cultured cell-derived rabies vaccine (CCDRV) protocol after the rabies diagnosis had been confirmed in the dog. The five other patients received CCDRV. In Marseille, risk assessment of these eight patients, based on World Health Organization (WHO) criteria [2] was as follows: category 1: 4 patients, category 2 and 3: 2 patients each (Table 1). Category 2 patients received CCDRV completion as well as category 1 patients considering that a full course of vaccine would provide preventive immunization in case of further travel to Algeria. One category 3 patient presented 21 days after the first vaccine was provided abroad at the time the administration of RIG in contra-indicated [3]. In this patient, we only completed his CCDRV course. The remaining category 3 patient presented 3 days after a course of SMBRV was started in Algeria. In this patient we
decided to start CCDRV and human RIG. Finally among the two patients who did not consulted in Algeria, one had a category 1 exposure and no RPEP was applied, the other had a category 3 exposure and was treated with CCDRV and human RIG. At the time of writing, all exposed patients are safe. From discussions with family members, we noted than none was aware of rabies risk in Algeria before traveling. Retrospective risk assessment was difficult because of biased memories of individual about the type of contact they had with the animal, and mostly because of the resulting stress regarding a deadly disease like rabies.

Rabies is still enzootic in Algeria [4], with 652–1212 animal cases reported yearly from 2004 through 2012 with most cases in dogs [5,6]. Over the same period of time 12 to 32 human cases were reported yearly [5,6]. Over 839 people died of rabies from 1970 to 2003 [7].

Several points should be underlined in this report:

1. A 10 person-family traveled in rural Algeria without seeking pre-travel advice, did not received pre-travel rabies immunization, and were exposed to a rabid dog including 8 within less than 4 days of arrival. This result is in line with most studies addressing RPEP in international travelers showing a low rate (10%) of pre-travel vaccination among rabies in injured travelers and that less than 10% of those in need for RIG received it in the country of exposure [8]. In a recent GeoSentinel studies conducted on 2697 international travelers with animal-associated exposure to rabies virus, a pretravel encounter with a health care provider was recorded for only 32% of patients and a pretravel rabies vaccination was reported by 11% of patients [9]. In this series, a short median duration of travel (2 weeks) was observed and 12% patients were migrants or their descendants visiting friends and relatives in their country of origin, representing the second most common reason for travel following tourism [9]. In a recent study in Australian travelers, an even lower 4% pre-travel complete course of vaccine was recorded [10]. In a review of 60 cases of rabies in international travelers, a significant proportion of the cases were observed in migrants or their descendants when emigrating from their country of origin or after a trip to visit friends and relatives or for other reasons (43%) [11]. Therefore, people visiting friends and relatives in dog rabies endemic areas is one of the greatest risk group of rabies exposure and the greatest risk group for rabies among travelers.

2. Criteria for rabies risk assessment and recommendation for RPEP differ between Algeria, and France. Notably, any exposure on face, head, neck, hands, feet and genitals, any exposure to wild animal, requires immediate vaccination and administration of rabies immune globulin.

3. SMBRV is still in use in Algeria although WHO strongly recommends that its production and administration be discontinued [2]. In a few countries, mainly in Asia and Latin America, populations at high risk for rabies still depend on

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### Table 1

Rabies post-exposure prophylaxis (RPEP) in 10 travelers exposed to a rabid dog in Algeria.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Gender/age (years)</th>
<th>Travel dates (day/month/year)</th>
<th>Period of exposure</th>
<th>Algerian classification</th>
<th>RPEP in Algeria</th>
<th>Time between first vaccine and presentation to Marseille center (days)</th>
<th>WHO classification</th>
<th>RPEP in France</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F/47</td>
<td>14/08/2016 – 06/09/2016</td>
<td>14/08/2016 – 18/08/2016</td>
<td>3</td>
<td>CCDRV (Zagreb) + ERIG</td>
<td>21</td>
<td>3</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>2</td>
<td>F/22</td>
<td>05/08/2016 – 29/08/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>CCDRV (Zagreb) + ERIG</td>
<td>21</td>
<td>2</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>3</td>
<td>M/33</td>
<td>05/08/2016 – 29/08/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>CCDRV (Zagreb) + ERIG</td>
<td>21</td>
<td>1</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>4</td>
<td>M/12</td>
<td>16/07/2016 – 25/08/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>CCDRV (Zagreb) + ERIG</td>
<td>21</td>
<td>2</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>5</td>
<td>F/60</td>
<td>05/08/2016 – 29/08/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>CCDRV (Zagreb) + ERIG</td>
<td>21</td>
<td>1</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>6</td>
<td>F/28</td>
<td>05/08/2016 – 30/08/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>Mouse brain vaccine (Zagreb)</td>
<td>7</td>
<td>1</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>7</td>
<td>M/64</td>
<td>07/08/2016 – 05/09/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>Mouse brain vaccine (Zagreb)</td>
<td>21</td>
<td>1</td>
<td>Completion of CCDRV (Zagreb)</td>
</tr>
<tr>
<td>8</td>
<td>F/32</td>
<td>06/08/2016 – 23/08/2016</td>
<td>09/08/2016 – 18/08/2016</td>
<td>3</td>
<td>Mouse brain vaccine (Zagreb)</td>
<td>–</td>
<td>3</td>
<td>CCDRV (Essen) + HRIG</td>
</tr>
<tr>
<td>9</td>
<td>M/10</td>
<td>08/07/2016 – 15/08/2016</td>
<td>09/08/2016 – 15/08/2016</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>3</td>
<td>CCDRV (Essen) + HRIG</td>
</tr>
<tr>
<td>10</td>
<td>M/34</td>
<td>12/08/2016 – 16/08/2016</td>
<td>12/08/2016 – 16/08/2016</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1</td>
<td>–</td>
</tr>
</tbody>
</table>

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a Algerian classification and indications for RPEP: category I contact - Touching or feeding animals, licks on the skin; requires no treatment, category II contact — nibbling of uncovered skin, minor scratches or abrasions without bleeding, requires immediate vaccination, category III contact — single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks, exposure to bat bites or scratches; any exposure on face, head, neck, hands, feet and genitals, any exposure to wild animal, requires immediate vaccination and administration of rabies immune globulin.

b World Health Organization classification and indications for RPEP: category I contact - Touching or feeding animals, licks on the skin; requires no treatment, category II contact — nibbling of uncovered skin, minor scratches or abrasions without bleeding, licks on broken skin; requires immediate vaccination, category III contact — single or multiple transdermal bites or scratches, contamination of mucous membrane with saliva from licks, exposure to bat bites or scratches; requires immediate vaccination and administration of rabies immune globulin.

c CCDRV: cell cultured derived rabies vaccine.
d Zagreb protocol (2 simultaneous intramuscular doses on day 1, 1 dose on day 7 and 1 dose on day 21).
e Equine rabies immune globulin.
f Algerian Mouse brain vaccine protocol in adults suffering category III injuries (1 subcutaneous periumbilical, 2 ml dose on day 1, 2, 3, 4, 5, 6 and 1 intradermal forearm 0.25 ml dose at two sites on day 10, 14, 24, 34 and 90).
g HRIG received it in the country of exposure [8]. In a recent study in Australian travelers, an even lower 4% pre-travel complete course of vaccine was recorded [10]. In a review of 60 cases of rabies in international travelers, a significant proportion of the cases were observed in migrants or their descendants when emigrating from their country of origin or after a trip to visit friends and relatives or for other reasons (43%) [11]. Therefore, people visiting friends and relatives in dog rabies endemic areas is one of the greatest risk group of rabies exposure and the greatest risk group for rabies among travelers.
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