Short Communication

Evaluation of Cases Admitted to a Center in Istanbul, Turkey in 2003 for Rabies Vaccination and Three Rabies Cases Followed Up in the Last 15 Years

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SUMMARY: We evaluated the cases of 7,266 individuals who applied to our hospital’s Center for Rabies Vaccination between January and December 2003. Among 1,831 female and 5,435 male cases, 37% were given 3 doses of vaccination, 14% were given 5 doses, and in 24% of cases a 2-1-1 vaccination schedule was applied. Antirabies serum of horse origin was given in 179 cases. Regarding the wounds, 83% were superficial and 17% were deep. Most of the cases involved dog bites (74%). Of the dogs involved, 30% were pets (with owners). Only a few (6%) of those pets had been vaccinated. Of the 2 dogs investigated for rabies in Pendik Veterinarian Research Institute, none were found to harbor the disease. In the last 15 years, 3 cases were followed up with a diagnosis of human rabies in our clinic. Domestic animals (without owners, living a somewhat wild life in cities) are still the cause of many rabies cases. As rabies carries a very high fatality risk, public health precautions and education are important as well as post-exposure prophylaxis.

Rabies, a viral infection primarily of carnivorous mammals other than human beings, is an acute disease of the central nervous system (CNS). It is transmitted to humans through an infected animal bite and almost always ends with death (1,2). With strict precautions, Western European countries have eliminated human rabies. According to data from the Turkish Ministry of Health, 655 human rabies cases in Turkey were reported from 1970-2003 (3). Unlike most infectious diseases, there is no effective medical treatment for rabies. Therefore, emphasizing measures of prophylaxis is important.

In a study, the World Health Organization (WHO) reported that dogs are responsible for 91% of reported cases of rabies in humans. The most important measure in controlling rabies is the regular immunization of domestic dogs and the impoundment of unconfined dogs (4). In the United States, Canada, and Western European countries, less than 10 cases of rabies in humans are reported per year; most of them are caused by either wild animal bites or else they are imported cases (5). Turkey occupies eighth place with a percentage of 5.2% relating animal rabies cases per 10 years. The percentage of human rabies cases caused by domestic animals is 98% in Turkey. In Turkey, domestic animal rabies is most frequently seen in big cities; Istanbul has an especially significant role, with 20% of the reported cases (6).

Post-exposure prophylaxis is administered to approximately 6 million people worldwide annually (7). Most clinical cases of rabies are seen in developing countries. In Turkey, post-exposure prophylaxis is administered to 50,000-100,000 persons per year (6). According to the Turkish Ministry of Health data, 110,624 animal bites with a risk of causing rabies were recorded in 2003 in Turkey. Of these cases, 12,827 occurred in Istanbul. The number of cases of rabies in humans has decreased to <10 since the 1990s, and only one case of rabies was reported in 2003 (4). For correct and effective prophylaxis, the area of contact, the depth and type of the wound, the potential risk of the animal, the immunization state of the animal and the patient, and the state of confinement of the animal should be known (8).

We retrospectively investigated the records of patients who were admitted to our outpatient clinic as a result of an animal bite or contact with suspected animals. Vaccination sufficiency was evaluated and the epidemiology and post-exposure prophylaxis procedures used in the three cases of rabies in humans observed during the last 15 years were interpreted. We evaluated the cases of 7,266 individuals who applied to our hospital’s Center for Rabies Vaccination from January 2003-December 2003. Age, sex, home address, telephone number, and the previous vaccination and antiserum administration states of each patient were recorded. The types of contact were grouped as direct (bites, scratches, contamination of mucous membranes or wounds with saliva of the animal), and indirect (contacts with a risk of contamination of injured skin by infected materials like touching, petting animals). Also, the time of exposure, the elapsed time interval after exposure, the depth of the wound (if it was a wound of the head, neck, hands or genital region, which carry a high risk), the existence of multi-site wounds, and the type of contact (direct skin or over clothing) were recorded. All patients were questioned about the species of the animal, if it seemed to have the potential to have rabies, the vaccination history of the animal, and if vaccinated the last date of vaccination. Any knowledge of the animal having bitten other persons, whether or not there was a provocation of the animal, and whether the animal could be observed for 10 days were also recorded. The need for prophylaxis for tetanus was evaluated.
in all patients in accordance with their ages and types of wounds.

In cases involving multiple or deep bites by animals suspected of having rabies or bites in risky areas, the injured area was cleaned thoroughly with soap and water and the wounds were treated with an anti-rabies serum of horse origin (after a sensitivity test), after which the standard vaccination schedules were initiated. Cases involving superficial scratches and bites carrying a low risk for rabies were treated with wound care and post-exposure vaccination without using rabies immunoglobulin (RIG). Patients were informed about the possibility of adverse reactions to RIG and the vaccine, and all allergic reactions were recorded. Surgeons were consulted regarding deep wounds needing suturing after RIG administration. If necessary, treatment with antibiotics was started.

Human diploid cell vaccine (HDCV) was administered for active immunization, and equine rabies immunoglobulin (ERIG) was administered for passive immunization. The exposure characteristics of the cases are shown in Table 1.

Most of the applications to our center for rabies vaccination occurred on the first day of the exposure (72%). This high rate is significant, as it shows that the grave consequences of this illness are understood by the community. The average number of applicants to our center seeking treatment after the wounds of this illness are understood by the community. The average number of applicants to our center seeking treatment after the first day of exposure was 605 per month, and 34% of the cases occur in the summer season. Out of 7,266 cases, only 6 cases definitely did not need vaccination. Most of the cases were males (75%) and one-third of the cases were under 15 years of age. The features of the wounds and vaccine administration schedules are shown in Table 2.

The fluorescent antibody test, Sellers’ staining and histopathological diagnostic methods were used at Pendik Veterinarian Research Institute for the diagnosis of rabies in animals.

Inactivated rabies vaccine prepared in vero cells, which was obtained from the Ministry of Health, was administered to all of our cases. The cases for whom 5 doses were planned and who started with the 2-1-1 vaccination schedule were evaluated again after a 10-day observation period of the animal, and their treatment was changed to 3 doses if the animal remained healthy. The 2-1-1 vaccination schedule was used in cases in which RIG could not be administered due to allergic test results, and in those in which we intended to induce an early antibody response because of late application to our center after the injury. A total of 1,751 cases who took the first dose of the 5 vaccine series or the 2-1-1 vaccination schedule and then discontinued were recorded as “incomplete vaccinees” and were reported to the Provincial Health Directorate.

ERIG provided by the Ministry of Health was administered to 179 of the patients. Two hundred and five cases were referred to surgery just after infiltration of the wound with RIG, because surgical closure of the wound was warranted in these cases. Antibiotics were prescribed in 211 cases involving deep wounds with a risk of developing infection. In addition, 2,333 patients (32%) received one dose of tetanus vaccine.

Three human rabies cases have been followed up in our clinic over the last 15 years. All of the three cases were admitted to our clinic, not immediately after the injury, but after clinical symptoms had developed.

Case 1: A 32-year-old shepherd, while running after a wolf that had attacked his sheep, fell on icy ground, and the escaping wolf stepped on his face, tearing his conjunctiva with its claw, in September 1989. Although he was vaccinated with HDCV on days 0, 3, 7, and 14, he was admitted to our clinic again with fasciculations in his face, aerophobia and hydrophobia, which started on the 14th day following the injury. Upon his first physical examination, he was conscious; saliva discharge from his mouth was observed because of increased salivation and defective swallowing. Then convulsions developed, the patient became agitated, and he died within 24 h. A short incubation period and very speedy clinical progress were observed in this patient because he was injured by a wild animal; RIG was not applied, although the vaccination schedule was started on time and the vaccinations were applied appropriately. The wound was very close to the CNS, and the injury was a mucosal injury.

Case 2: A 40-year-old man was admitted to our clinic in November 1989 with aerophobia, hydrophobia, and anxiety. Four months ago, while he was trying to take a puppy away from his children, he had a contact with the dog that he hardly remembered. He was not bitten by the dog, but his hand was contaminated with its saliva. The patient was a construction worker in buildings which suggested that he may have had injured skin on his hands. He did not have any vaccination history. The patient died 48 h after hospitalization.

Case 3: In August 1990, a 67-year-old man had been bitten on his wrist while playing with his pet dog and 3 doses of Semple vaccine were administered. After a while his dog was

Table 1. Characteristics of the exposures and the wounds

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<tr>
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<th>n (%)</th>
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<tbody>
<tr>
<td>Dog bite</td>
<td>5,390 (74)</td>
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<tr>
<td>Cat bite</td>
<td>1,850 (25)</td>
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<tr>
<td>Other animals</td>
<td>25 (0.3)</td>
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<tr>
<td>Pet of known origin</td>
<td>2,150 (30)</td>
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<tr>
<td>Animals without owners</td>
<td>5,120 (70)</td>
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<tr>
<td>Deep wounds</td>
<td>1,250 (17)</td>
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<tr>
<td>Superficial wounds</td>
<td>6,010 (83)</td>
</tr>
<tr>
<td>Head-neck wounds</td>
<td>298 (4)</td>
</tr>
<tr>
<td>Trunk-extremity wounds</td>
<td>4,610 (63)</td>
</tr>
<tr>
<td>Hand wounds</td>
<td>2,360 (32)</td>
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</tbody>
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1: Species of the animal responsible for the bite.
2: Ratio of animals with owners.
3: Depth of the wound.
4: Wounded body region.

Table 2. Characteristics of the vaccine administration schedules

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<tr>
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<tr>
<td>First day admission</td>
<td>5,320 (72)</td>
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<tr>
<td>1-5th day admission</td>
<td>1,890 (26)</td>
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<tr>
<td>After 5th day admission</td>
<td>146 (2)</td>
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<tr>
<td>3 doses in 10 days</td>
<td>2,690 (37)</td>
</tr>
<tr>
<td>5 doses in 30 days</td>
<td>1,050 (14)</td>
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<tr>
<td>2-1-1 schedule</td>
<td>1,770 (24)</td>
</tr>
<tr>
<td>Number of patient not completing the standard vaccination schedule</td>
<td>1,750 (24)</td>
</tr>
<tr>
<td>No vaccine required</td>
<td>6 (&lt;1)</td>
</tr>
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1: Time to hospital admittance after exposure.
2: Vaccine administration schemes.
wounded by other dogs and he took it to a veterinarian after he dressed the dog’s wounds. The dog died of an allergic reaction following an injection of one dose of penicillin. The patient discontinued his own vaccination. Four months after the injury, he developed symptoms of anxiety and hydrophobia, and he sought medical care at our clinic. At the time of his hospitalization, he could hardly overcome his hydrophobia. His anxiety and restlessness increased and convulsions developed. Under general paralysis, he died on the 8th day after his hospitalization.

Rabies is a zoonotic disease and remains a significant public health problem in Turkey. The only protection methods are to avoid contact with animals and post-exposure prophylaxis. In developing countries like Turkey, domestic animals without owners living a somewhat wild life in urban areas are still the causes of most of cases of rabies. Therefore, all bites are suspected to carry a potential risk for rabies, and this increase the number of vaccinations. According to statistics from the Ministry of Health, 12,827 bites carrying a potential risk for rabies were reported in 2003 in Istanbul (4). From 1996-2003, the median number of cases per year in which a regime of prophylaxis was administered was 12,000 in Istanbul (9).

In a study from China, the human rabies cases recorded from 1984-2002 were reported. It was found that while the number of cases per year was about 4,000-6,000 before 1990, there was a decrease in the number of cases after 1990. The lowest number (159) was observed in 1996, but the number of cases has increased since 1998. This increase was attributed to the increase in the number of dogs, low vaccination rates, incorrect treatment of injuries, and a lack of cooperation between health centers (10). In the United States, a total of 7,967 animal and 3 human rabies cases were reported in 2002 from 49 states and Puerto Rico. This represents a 7.2% increase compared to the preceding year. More than 92% of them occurred in wild animals (animals living a wild life in rural areas) and only 7.4% were domestic animal (pets with owners) rabies cases (11).

It has been shown in animal experiments that wound care performed using a 20% soap solution and, if necessary, wound debridgement decrease the risk of developing clinical illness by approximately 90% (2). Wound treatment was performed in all of our cases, and, if necessary, antibiotic treatment was added. The prophylaxis schedule of the WHO consists of three steps: (i) Local treatment of the wound, (ii) administration of human rabies immunoglobulin (HRIG) or ERIG, and (iii) effective vaccination (12). The immunogenicity of the Semple vaccine is generally weak, and the antibody response is delayed. Our third case was vaccinated with Semple vaccine but had not completed his vaccination schedule. Clinical symptoms developed after a long incubation period and the disease ended fatally. In a report from Haydarpaşa Numune Hospital, an 18-year-old woman was bitten on her nose and eyebrow superficially by a dog, and even though Semple vaccine was started on the day of the contact, after a 75-day of incubation period, the symptoms of rabies appeared, and she died after a follow-up of 4 days (13). Also, the Semple vaccine may be associated with serious neurological complications (14).

In the seven rabies cases followed up by Goktas and his colleagues (13) from 1989-1993, the incubation period varied between 17 and 150 days. In these cases, the patients died 2-18 days after the appearance of the symptoms. HDCV and ERIG were administered after contact to the individual who survived for 18 days, but after a 17-day incubation period, clinical disease developed, and the diagnosis was also confirmed at autopsy. In our first case, HDCV was administered without RIG. Studies have shown effective protective antibody levels on the 14th day of HDCV administration (15). In our practice, the vaccination regimen could be discontinued if the animal involved remained healthy after an observation period of 10 days. In all cases, the vaccine was administered into the deltoid muscle. Allergic reactions due to the vaccination were not observed in our cases. In order to lower the cost and produce a quicker antibody response, another administration schedule, a 2-1-1 regimen, known as the Zagreb regimen, can be applied (16). This schedule is preferred particularly when there is a delay in the treatment, if RIG is not available, if there are multiple injuries in high risk areas, and for patients with immunodeficiency (8,13,17).

Domestic animal bites are seen quite frequently in our region, especially in certain districts. Preventive measures should be improved and taken more seriously in both our institution and by the society at large. The effective control and immunization of animals may cost less than the vaccination of potential rabies cases. Vaccination indications should be evaluated properly, and cases must be followed up seriously. The population and especially children should be informed about rabies and about preventive measures that can be taken against it. The owners of domestic animals must be made conscious of their responsibility for the animals beyond just feeding them.

**REFERENCES**