PREVENTION OF HUMAN RABIES

Treatment of Persons Bitten by Rabid Wolves in Iran

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SYNOPSIS

Treatment by the classic methods of persons bitten by rabid wolves gives results, but these results are unsatisfactory: the case-fatality-rate is decreased, but only to an inadequate extent. New and more effective methods are indisputably required.

In the course of 13 years, 325 persons bitten by wolves have been treated at the Antirabies Service of the Institut Pasteur, Iran; almost all, namely 307, had bites of exceptional severity, only 18 having superficial wounds. In 186 cases the bites were on the face, skull, or neck, in 74 cases on the upper limbs, in 5 cases only on the lower limbs, and in 60 on the trunk.

From 1936 to 1946 the vaccine used for treatment was one of the Pereira de Silva type (phenolized rabbit-brain); after 1946 a vaccine of the Semple type (sheep-brain) was employed. Tests were also made using Ferran’s hyperintensive method; other trials were carried out with respect to the increase, repetition, and prolongation of the doses.

The results of the treatment must be considered as disastrous. Out of the 325 persons treated, 60 died of rabies, i.e., 18.5%, within periods of time indicating failure of the method. In point of fact, 127 persons who had been bitten arrived at the Institut Pasteur from one to seven days after the bite: 35 of them, i.e., 28%, died. Out of 186 persons bitten on the head, 53, i.e., 28%, developed rabies.

Several viruses were isolated, either from the wolf brain, or from the brains of persons dying in the course of treatment. None of these viruses differed appreciably from the street virus isolated from dogs in Iran or in other countries; none of them showed any special virulence or aggressive potency. Consequently the failures observed must be attributed to the

severities of the bites and above all to their size, since the case-fatality rate among the 74 persons bitten on the arm was only 9 5% and fell to zero for the 65 persons bitten on the trunk or legs. In the case of certain grave bites, exceptionally short incubation periods were observed: in two cases rabies developed 11 days after the bite, in one case less than 5 days after a grave bite on the head. The most frequent incubation period is 18-25 days, more rarely it is 26-40 days and only exceptionally 41-45 days.

Experimental treatment with hyperimmune serum carried out at the request of the WHO Expert Committee on Rabies over the course of the past two years has not given good results because the conditions imposed for the tests with respect to the period elapsing since the bite were too exacting.

We should like to make the following comments on the above facts and figures:

1. Since, because of the very conditions existing in regions still infected by wolves, the presence of rabies can be proved in the wolf causing the bite only in exceptional cases, all persons attending our antirabies service after having been bitten by wolves have been systematically treated. However, many of the wolves causing bites are not rabid, and we may quote as an example a small town, Zerjijn, in the mountains, near which in 1951 there was a pack of about 35 wolves, led by a particularly audacious old male. Although this town is very busy and populous (50,000 inhabitants) and traversed by a main road over which numerous motorways pass by day and night, the wolves on several occasions came down and attacked the town during the night or the early hours of the morning, making off with several young children even from the courtyards of the houses, and would also make more than 40 people during various pathologic habitats between them and the inhabitants, until an extensive "battled" freed the region from their depredations. There was not a single case of rabies among the people bitten.

The inhabitants of these regions are perfectly familiar with rabbits and readily recognize the symptoms in the wolf. They do not mistake an attack by a pack of this nature, or the defence of a female surprised in her lair, or the curious intuitions of hungry wolves in winter, with the sudden attack of a well-known and trusted individual, which is always taken place in daylight in the middle of the village and ends, after a frightful struggle, with the death of the wolf under the sticks and picks of the peasants.

As these cases almost invariably occur in mountainous villages, those bitten must generally themselves reach a decision whether or not to come to Tehran for treatment, and usually, when they consider it certain that the wolf or wolves causing the bite were not rabid, they remain in the village and the story becomes known only much later. However, if there is an official authority in the village or a representative of the central government, even if simply a policeman, those bitten are sent, despite their resistance, to the hospital instead.

Clearly a certain number of the "series" figures in our statistics 1 of this nature and as a matter of fact, in all cases in these series in which the persons concerned stated that the animal causing the bite was not rabid, no death occurred.

The average death-rate of 18.5% which we indicate in accordance with the usual statistical practice, consequently does not precisely correspond to the actual state of affairs. On eliminating the series (and these series only) where the biting wolf was very probably not rabid and where no death occurred, we arrive at a case-fatality rate of about 22%.

2. If we consider only those series where the presence of rabies in the biting animal has been proved by the death of one or more of these bitten, eliminating on this occasion all series where no death has occurred, we arrive at a case-fatality rate of about 25%. Among those bitten on the head the figure becomes 42%.

3. Considering only cases treated without marked delay we reach a still higher total, namely 28%.

Discussion

What is to be made of these figures? It is well known that statistics, although they are irrefutable, have been used by the opponents of anti-rabies treatment to disparage its value, solely because it is going so far as to affirm that without treatment the case-fatality rate would probably be 50% higher. Nicolle 2 has recently presented new historical and current data on the treatment of persons bitten by rabid wolves. His paper, based on documentation from several countries (including Iran) and retaining only thoroughly screened results — i.e., cases of bite in which there was proof of rabies — is an absolutely rigorous analysis, displaying the most strictly critical attitude towards the treatment. On the basis of scientifically reliable documents published before the discovery of antirabies treatment, Nicolle arrives at a case-fatality rate of 64%, i.e., 103 deaths out of 169 persons bitten. In comparison with this figure, and using, as already mentioned, only occasions of indisputable reliability, the author cites 236 cases of bites treated by various methods with only 6 deaths, i.e., 27%, which figure is almost identical with the one we have given above for our observations extending over 13 years in Iran, after reviewing the statistics concerned.

It would seem, therefore, that even when the most critical attitude possible is adopted, the figures speak definitely in favor of treatment whatever the method employed, since the case-fatality rate is reduced by more than half.

2. Nicolle, M. (1925), Z. Hyg. 152, 39,
The only figure which might be open to question is the death-rate among those not treated, for which Nicole has adopted the figure of 61% in accordance with old documents.

However, in this connection mention may be made of a tragic occurrence which recently took place in Iran, and was reported by Grenzina, a German physician in charge of a clinic in the south of the country. A group of 32 persons bitten by the same rabid wolf remained without treatment, for reasons which Grenzina summarizes as follows:

"According to the Health Ministry instructions, bitten persons who are relatives regard the bite too, be it as rapidly as possible to the local health authorities at Tehran for vaccination treatment. However, the implementation of this regulation is reported by those who visited the author and the published report of the Ministry of the Animal population. Consequently, of the 32 cases described by 19 could be made to Tehran for treatment, using force, and with considerable delay."

Of these 32 persons, 15 died of rabies; the statistical data derived therefrom by Grenzina are, however, falsified by an error which we have requested him to correct in a coining number of the journal concerned. His group B, i.e., the 6 persons he sent to Tehran 11 days after the date of the bite, actually only arrived there 23 days after that date. In view of this delay, the bitten persons cannot be considered as treated, and those among them who survived cannot be included in the statistics, as Grenzina has done. Furthermore, the author arrived at a diagnosis of rabies on the basis of clinical symptoms in the case of 2 of the 6 bitten persons after 8 and 9 days' incubation, whereas in reality these 2 patients only developed clinical signs much later, namely after 18 and 30 days respectively. His conclusions are consequently invalidated as concerns both the average incubation figures and the case-fatality-rate; the average case-fatality-rate should be 47% instead of 53%.

It may be said that, although this figure of 47% is much lower than that accepted by Nicole (61%), it still remains very different from the most probable one which we have given, namely 27%. The case-fatality-rate among persons bitten on the head doubles (54%) in the series given by Grenzina, whereas it is 47% in Nicole's statistics, and 42% in our own corrected statistics.

If this is so, why have we nevertheless used the phrase: "The results of treatment must be considered as disastrous!"? It is because, in an instance such as ours, which can show extremely satisfactory figures as regards canine rabies—since in the course of 12 years only 9 persons bitten by rabid dogs have died after treatment—the survival of such a group of bite-wound victims represents a real disaster. We know that inevitably several of these terrified married people will die of rabies, despite the ritual gesture of treatment.

Consequently it is useless to compare statistics and to congratulate ourselves on having reduced deaths among those with head wounds; for example, by 10% or 15%, it cannot be disputed that from the antibacterial treatment of persons bitten by rabid wolves is considered a failure by everyone.

Conclusions

Men it be inferred that the very principle of antibiotic treatment is in doubt? In no way: we can only conclude that the treatment in its present state, and whatever the vaccine so far used, is not sufficiently effective.

FIG. 1. TYPICAL SEVERE WOLF BITES ON HEAD AND NECK OF A PATIENT

Thus, as we have said, it is to the severity of the bite and their site (see Fig. 1 and 2) that the failure of treatment in the case of those bitten by rabid wolves must be imputed. Those locations where the virus is deepest in the skin and has infiltrated the deepest layers of the skin surface, result in massive inoculation to the bite of the large chondral spine humps. In the case of more severe bites, treatment seems to give much more favourable results, comparable to those obtained with dog bites. That, although we have given above a figure of only 9% for the case-fatality-rate among 34 persons bitten by the arms, and although after the slightest tetanization this figure cannot be put at more than 15% in the series observed by Grenzina 3 people out of 19 bitten on the arms, i.e. 37%, contracted rabies.
It is in an attempt to remedy this insufficiency of the method of treatment that we have undertaken for the past three years, on behalf of WHO, experiments in the treatment with hyperimmune serum of cases of wolf bites, at first only with persons presenting themselves less than 72 hours after the bite, and then, in recent months, systematically in all cases of bites by wolves. The results of these trials, which are not yet evaluable, will be made known in due course.

However this may be, the position is as follows: antitoxin treatment in its present form is perfectly valid in principle but is not sufficiently effective. The problem of its treatment cannot continue indefinitely to be viewed in the rosy light of study favourable statistics, particularly those of countries where rabies no longer exists. Future developments should favour research aiming at the production of more active antitoxins in small volume, of powerful antibodies, or, better still, of avirulent living viruses which would resemble Pasteur’s discovery its original significance.

RESUMÉ

Depuis 1959, 125 personnes ont été guéries dans 707 cas de rage. Ces 125 personnes ont toutes reçu l’hyperimmunisé antirabique. Les traitements ont été effectués au Service antirabique de l’Institut Pasteur de l’Iran, dans le but de réduire la mortalité des malades atteints de rage. Les malades ont été traités en appel de rage et après que le virus a été éliminé par la rage. Les malades ont été soignés par le Dr. Darabi, le Dr. Darabi et le Dr. Darabi. Des cas de rage ont été traités par le Dr. Darabi, le Dr. Darabi et le Dr. Darabi. Des malades ont été soignés par le Dr. Darabi, le Dr. Darabi et le Dr. Darabi.