MONKEY-BITE ENCEPHALOMYELITIS

REPORT OF A CASE—WITH RECOVERY

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Those who handle monkeys are frequently bitten, usually without untoward results. Exceptionally, however, disaster may follow. Sabin and Wright (1934) first recorded a case of acute encephalomyelitis in a doctor who had sustained such a bite. Within three days vesiculo-pustular lesions developed at the site of the bite followed by regional lymphangitis and adenitis. A week later signs of motor and sensory disturbances began in the legs and bladder, and these were followed by an acute ascending myelitis. Death in respiratory failure occurred in a few days. From lesions in the cord, brain, and spleen a strongly neurotropic filterable virus was isolated which they named "monkey B." Sabin (1949) also reported a second case with a somewhat similar history, course, and termination, though there had been no bite and infection had presumably resulted from contamination of a laceration on the right hand with infected monkey saliva. A similar virus was again recovered.

Olitsky and Casals (1952) referred to two similar cases following monkey-bites; but they were not reported, but were presumed to be virus B infection; both showed encephalitis; both were bitten by monkeys prior to the disease; both, however, were not studied for virus isolation (Olitsky, 1958, personal communication). Sabin (1958, personal communication) believes that he has now traced 10 additional cases retrospectively, one of which recovered with severe disability. We have knowledge of one fatal case in this country, while two other fatal cases have been reported from Canada (*The Times*, March 22, 1958). How many of these have been studied virologically is unknown and none has been published. The following is the first complete account of the natural history of the disease, as well as the first recovery to be recorded. This is the more pertinent, since it is now clear that monkey-bite encephalomyelitis is not only a lethal but an increasing hazard.

(Virus B appears to be closely related to the herpes simplex virus of man, of which, indeed, it may be regarded as the simian variant. Most commonly it causes shallow ulceration on the dorsum of the tongue, though ulceration may occur elsewhere in the mouth or pharynx. Rarely it excites a vesiculo-pustular eruption on the lips. An important point is that the animal appears quite well, although at post-mortem examination the tracts of the cranial nerves may show multiple infiltrations by microglia surrounding cells containing what appear to be inclusion bodies. In tissue culture, virus B causes typical ballooning of the cells, frequently resulting in the formation of giant cells.)

Case Report

A monkey-handler aged 31 had been immunized against poliomyelitis in midsummer, 1957. On September 24 he was bitten in turn by two apparently healthy monkeys, once on the terminal phalanx of the left index finger and once on the dorsum of the third left finger. Both lesions were made to bleed and washed under the running tap, following which tincture of iodine was applied. They healed uneventfully. On September 30 he was vaccinated against influenza. On October 7 he went to his doctor complaining of a pain between the shoulder-blades, which the following day developed into a left-sided girdle pain and later passed off. (This was attributed to the vaccination against influenza.) For the next few days, apart from a headache, he felt well, but on October 13 his left leg gave way at work and he was sent home as a case of influenza. On the following day he could scarcely walk and was unable to pass water. He was sent to hospital as a suspected case of poliomyelitis.

When seen by one of us (G. E. B.) at Maidenhead Isolation Hospital on October 16 he was febrile but conscious and co-operative. He had been vomiting frequently. He could not sit up, but could bend his head freely—there was no true meningism. Pupillary reactions were normal, but there was marked anisocoria, with twitching of the face and trembling of the tongue. The abdominal reflexes were present. The left arm was weak and the triceps-jerk absent. The right arm appeared normal, but the reflexes were grossly exaggerated; the muscles of the back, pelvis, and abdomen were also weak; the left leg was almost immobile, with absent jerks; the right was weak and the reflexes were reduced; the plantars were equivocal. In addition there was loss of touch, pain, and vibration sense over the left lower leg and ankle, and a patchy loss of sensation over the lower half of the body generally. A lumbar puncture showed a clear fluid containing 75 cells per c.mm.; protein, 80 mg. per 100 ml.; sugar, 68 mg. per 100 ml. His was clearly not a case of poliomyelitis, and, in view of the history, the possibility of virus B infection had to be considered.

Two days later (October 18), because of developing weakness of respiration, he was transferred to the South Middlesex Hospital. On admission paralysis was found to have progressed. In addition to the signs previously noted there was weakness of the intercostals and of the left leaf of the diaphragm, and the vital capacity was down to 2 litres. The abdominal reflexes too were now absent. Both lower limbs were extremely weak, with absent reflexes, and the reflexes were also reduced in the left arm. The right arm still seemed normal, with increased jerks. There was now some left facial weakness, and, though the anisocoria had disappeared, there was marked nystagmus on looking upwards and to the right. Sensory loss over the lower half of the body was widespread and retention of urine was absolute. In the hope that it might contain some relevant antibody, he was given 10 ml. of human gamma-globulin.

On the morning of October 19 his vital capacity had fallen to 800 ml. and respirations were rapid and shallow. He was placed in a tank respirator and at first settled down well. High pyrexia continued, however, and vomiting was frequent. His vital capacity continued to fall—to 460 ml. at 8 p.m. At the same time his voice became hoarse, and pooling of secretions in the pharynx necessitated frequent suction. He was therefore removed from the tank respirator and, under general anaesthesia, a tracheostomy was made, a cuffed endotracheal tube was inserted, and he was placed on intermittent positive-pressure respiration, using a Radcliffe respirator. As the nose was impassable to a catheter, an intravenous drip was set up in which cortisone, 100 mg., was incorporated. A further 10 ml. of gamma-globulin was also given.

As is common in such cases, progress during the following week was somewhat chequered, though eventually the patient settled down fairly well. During the week, cortisone,

200 mg. daily, was administered by intramuscular injection, antibiotic cover being maintained. The temperature fell by slow lysis. Limb paralysis was now almost complete, with absent reflexes all round; facial weakness was notable and nystagmus pronounced. Fortunately, some improvement in swallowing soon began, so that by October 26 fluids could be taken by mouth and by October 29 semi-solids could be taken as well; intravenous maintenance was therefore discontinued. Shortly thereafter some increase in motor power in the limbs generally was noted, but painful involuntary spasms appeared in the left leg. On November 7 the patient went for two minutes without assistance to respiration, and breathing power continued to improve until November 9, when it was interrupted by massive collapse of the left lung which was cleared only by vigorous physiotherapy. Thereafter respiratory capacity increased slowly but steadily, and it was possible to substitute a rocking-bed for positive-pressure respiration for short periods. General progress was much influenced by an intractable bladder infection, at first with *E. coli* and later with *Pseudomonas pyocyanea* requiring treatment with polymyxin B. The pressure points also gave trouble, and an intractable bedsore developed over the sacrum which demanded the use of a ripple mattress. Daily enemata were also necessary. On November 8, for the first time, he felt an injection into the right buttock.

The patient's psychology presented a curious parallel to his physical condition. At first he was well controlled if occasionally confused, and he was always an unsatisfactory witness for sensory evaluation. When placed in the tank respirator he was fairly calm, but a few days later he became increasingly irritable, excitable, and emotional, often weeping spontaneously. Subsequently he stated that he had no memory of events from the time he was placed in the respirator on October 19 until about November 15. After that date, though still highly emotional, irritability diminished markedly, but he continued very apprehensive, thereby delaying his weaning from the respirator considerably. About November 15 bladder control became re-established. Gradual improvement in breathing resulting in a vital capacity of 2 litres enabled artificial respiration to be discontinued on December 9. About this time reflexes and sensation also began to appear in the limbs, and by January 15, 1958, power was regained almost fully in the right arm and leg and to a considerable extent in the left arm. The left leg, however, remained sharply contracted and tremulous and apt to go into painful clonic spasms on the least stimulation. On passive extension it gave a sensation reminiscent of that encountered in cases of post-encephalitis lethargica. The plantar reflexes remained extensor. By now the left facial nerve had quite recovered and the pupils were normal, but there was still some fine residual nystagmus, especially on looking upwards.

On January 27 the patient was transferred to a long-stay hospital for further rehabilitation. The latest report (April 9) stated that he was quite fit, and with elbow crutches and a full-length calliper could walk 25 yards without aid. The power in his arms was back to normal. There was no sensory disturbance left and bladder control had entirely returned. The spasm in the left leg was progressively diminishing and there was every indication that he would be able to resume an active life and return to full work in due course.

Comment

The picture is consistent with a virus infection which ascended along the peripheral nerves to the cord, producing widespread foci of inflammation throughout the whole central nervous system. It is remarkable that signs were much more pronounced and lasting on the left (the bitten side) than on the right, which recovered much more rapidly. Lesions appeared to affect the long tracts mainly, the anterior horn cells escaping undamaged. Sensory changes, while at one time widespread, also proved transitory.

Psychological changes were also notable—irritability and gross emotional lability. There was amnesia for a period of about three weeks. The patient's intelligence seemed to be unimpaired.

The value of the gamma-globulin and of the cortisone given in treatment is difficult to assess. Even if the former contained significant quantities of herpes simplex antibody valid against virus B, it would appear (by analogy with other virus disease) to have been given much too late to exert any appreciable influence on the course of the condition. From the time that cortisone was administered, the march of the paralysis appeared to halt and the temperature returned to normal by a slow lysis, but there was no dramatic fall such as is commonly seen in other conditions where it has proved effective.

A NOTE ON VIROLOGY

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Attempts to isolate the causal agent from faecal and serum samples and determinations of virus B neutralizing antibody on acute and convalescent sera were carried out. All tests were run in monolayer tissue cultures of monkey-kidney tissue, employing a method outlined previously (Tyrrell, Keeble, and Wood, 1956). Samples of faeces were prepared for inoculation by making a 10% suspension in normal saline and clarifying by centrifugation at 2,500 r.p.m. Serum samples were titrated against two strains of virus B—one isolated at Sefton Park, the other isolated in Canada in 1953 (Wood and Shimada, 1954).

Specimens.—Faecal samples were obtained on October 16 and 28, 3 and 15 days respectively after onset of illness. Serum samples were obtained on October 16 and 21, Novem- 8, and January 21; 3, 8, 26, and 100 days respectively after onset.

Results.—Tests for virus isolation on both faecal samples and the first three serum samples were negative. The final serum sample was not tested for presence of virus.

The virus B antibody titres in the four serum samples were as follows: day 3, 1:16; day 8, 1:25; day 26, 1:48; day 100, 1:32.

Conclusions.—Failure to isolate virus B from faecal samples is considered of no significance in that the route of infection via a wound would not necessarily involve alimentary infection. The results of the antibody tests are difficult to interpret, as we are ignorant of the degree to which neutralizing antibody develops in humans recovering from a virus B infection. It is also possible that the administration of cortisone in this patient depressed the antibody response in convalescence. However, a moderate rise in antibody did occur between the third and 20th days which, if considered in conjunction with the clinical data, suggests virus B encephalomyelitis as a probable diagnosis. It should be remembered, however, that monkeys may harbour many different viruses whose potentialities for causing disease in man are not yet fully known, so that it is not impossible that a virus of monkey origin other than virus B may have been responsible for this patient's disease.

Summary

A case of encephalomyelitis following monkey-bites is described. After a very stormy illness necessitating tracheotomy and intermittent positive-pressure respiration the patient made a good recovery and should be able to return to an active life.

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