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HUMAN MONKEYPOX TRANSMITTED BY A CHIMPANZEE IN A TROPICAL RAIN-FOREST AREA OF ZAIRE

MUTOMBO WA MUTOMBO I. ARITA
Z. JEZEK

Monkeypox Surveillance Team, Zaire, and Smallpox Eradication, World Health Organization, Geneva, Switzerland

Summary A case of monkeypox infection in a six-month-old baby girl who had been bitten by a wild chimpanzee in Kivu, Zaire, was investigated. The child had not been exposed to any monkeypox-like disease and no cases of such disease had occurred in the surrounding area during previous months. The time of onset of rash was consistent with the virus having been transmitted from the chimpanzee. However, it is still not known whether chimpanzees and other primates or lower mammals are the primary reservoir of monkeypox infection.

Introduction

HUMAN monkeypox is a zoonosis which occurs sporadically in the tropical rain-forest of west and central Africa. The virus was first recognised through outbreaks in captive monkey colonies at the State Serum Institute, Copenhagen, in 1958;[1] monkeypox virus, which belongs to the orthopoxvirus group, was isolated from the affected animals. Between then and 1968 there were monkeypox outbreaks in captive monkeys in a further nine laboratories in Europe and North America.[2] Since 1969 there has been no report of monkeypox in laboratories, despite intensified surveillance by laboratory staff handling animals, nor, since 1958, of monkeypox among wild animals in tropical forest: it is assumed, however, that laboratory-associated outbreaks must have resulted from infection introduced by wild monkeys shipped from tropical zones.

In 1970, a smallpox-like disease was discovered among the human population in Equateur Region of Zaire, where smallpox was believed to have been eradicated.[3] The subsequent study revealed that the patient had been infected with monkeypox virus. During the past twelve years, 79 cases of human monkeypox infection have been reported. Since the clinical illness closely resembles smallpox, the disease is the most important orthopoxvirus infection for World Health Organisation's programme of post-smallpox eradication surveillance.

Despite careful field investigation of the 79 cases, the source and reservoir of infection as well as the mode of transmission remain unknown. The disease is not readily transmitted from person to person. Monkeys are suspected to be the reservoir of monkeypox virus causing human infection, but this has never been proved. However, we now report an unusual episode of monkeypox infection in a baby in Kivu, Zaire.

Area

The case occurred in a small village called Kibwe (population 30) situated between latitude 1°15′ and 2°15′ south of the equator, in Kivu Region, Zaire (fig. 1). The village is in the administrative zone of Punia which has an estimated population of 60 000, in an area of 20 000 km^2. The entire zone is covered by tropical rain-forest. September to April is the rainy season and the rest of the year is dry. Chimpanzees, gorillas, baboons, various other monkeys, and wild rodents, including squirrels, are present throughout the area. In 1977, a human monkeypox case in a locality called Selibo II was treated in Katanti dispensary (fig. 1).

Case-report

On May 30, 1982, a mother of three children was hunting monkeys in a cassava field 1 km from Kibwe village, which is surrounded by dense tropical rain-forest; her five-year-old and six-month-old daughters were at the other end of the field. The mother suddenly heard screaming and saw that a large chimpanzee had taken the baby from her sister and was running into the forest. The mother pursued the chimpanzee and after a chase lasting about an hour, she finally managed to recover the baby which the fleeing chimpanzee had dropped. However, the baby was severely injured; she had been bitten by the chimpanzee on the left foot and had a fracture of the left femur. The mother reported that the face of the chimpanzee had been covered by ash-coloured dust and that some of the hair on its trunk and extremities was missing.

The baby had never been vaccinated against smallpox. On June 5 she became feverish, and on June 12 a generalised rash developed. On June 14 the mother, suspecting that the baby had smallpox, took her to the Lwenga dispensary, 30 km from Kibwe village. The nurse at the dispensary also suspected smallpox, and on June 16 the baby was taken by car to Lulingu Hospital, 70 km from the dispensary. The hospital doctor observed that the rash was at the pustular stage and was more densely concentrated on the face and extremities than over the trunk. On Sept. 1, the Zaire monkeypox surveillance team examined the baby, who still showed hypopigmented scarring (fig. 2); she had 70 spots on the face, 400 on the arms, 200 on the trunk, 525 on the legs, 50 on the soles, and 15 on the palms. The hospital physician (on June 16) also observed bilateral inguinal lymphadenopathy, more prominent on the left. The date of appearance of the inguinal lymphadenopathy and whether it appeared before or after the rash and fever is not certain. However, the mother stated that the swelling had appeared first in the left inguinal region. On June 20 bilateral submandibular lymphadenopathy became apparent.

On July 7 the last scabs fell off and the patient was discharged. The date of disappearance of lymphadenopathy is not certain, but when the surveillance team examined the patient 10 weeks after the onset of the rash, there was no lymphadenopathy. The type and distribution of rash and the appearance of lymphadenopathy are consistent with human monkeypox.

Results

Laboratory Diagnosis

A crust specimen was taken by the hospital staff and was sent to the WHO Collaborating Centre, the Centers for Disease Control, Atlanta. Examination by electron microscopy revealed poxvirus particles, and monkeypox virus was subsequently isolated on the chorioallantois of the chick embryo.

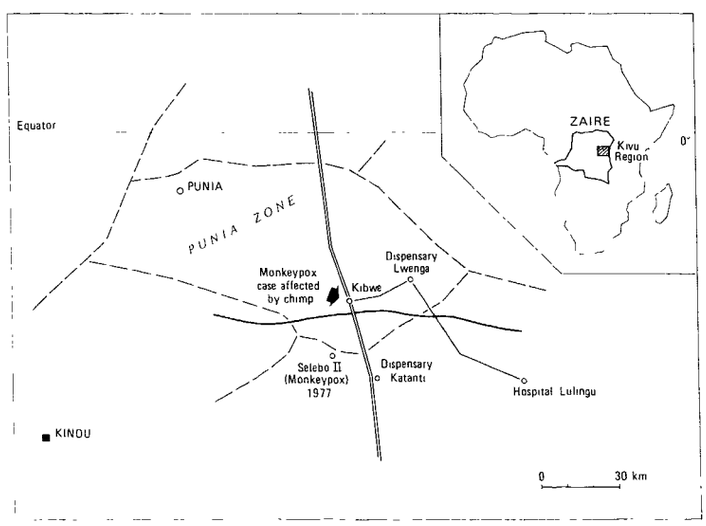

Fig. 1—Punia zone, Kivu, Zaire.

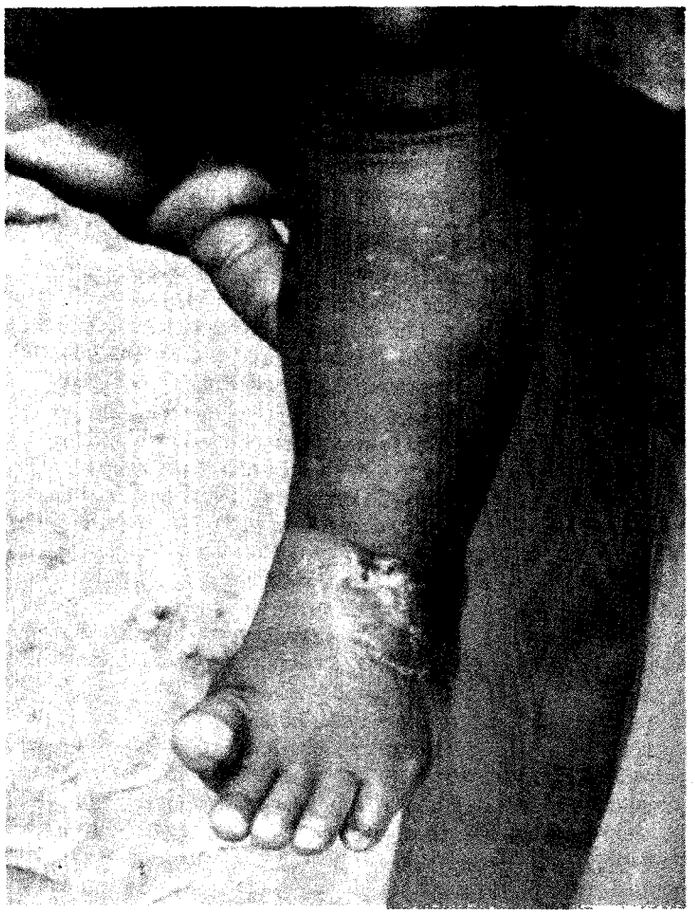

Fig. 2—Left foot showing healed bite and depigmentation caused by the rash (10 weeks after onset of rash).

Epidemiology

The Zaire monkeypox surveillance team conducted a special investigation in the area from Aug. 30 to Sept. 2, interviewing the mother, her family, and the staff of the dispensary and the hospital where the baby was treated.

The taking of a human child by a chimpanzee is a very rare occurrence. Indeed, the villagers themselves were astonished by the event and believed that an evil spirit had taken the form of a chimpanzee and kidnapped the child. Chimpanzees in the area are not fed as pets. Although the accuracy of the mother's statement was not initially in doubt, the surveillance team was able to confirm the report and observed that the appearance of the lesion was consistent with having been caused by a chimpanzee bite. It was confirmed that the baby had neither travelled outside the area nor been in contact with a patient with rash during the three weeks preceding the appearance of the rash. The family reported having eaten a sheep a few weeks earlier which had been healthy when slaughtered.

An investigation was conducted to discover whether there had been any similar illness in the area around the time of the baby's illness. The family, consisting of six members, was interviewed and examined. None had experienced a similar disease. All had been vaccinated, except for a three-year-old child from whom a serum specimen was taken. Subsequent testing of this serum sample by the W.H.O. Collaborating Centre revealed that the child did not have antibody against monkeypox or varicella viruses. The search for other persons with illness and rash was extended to the other inhabitants of the village of Kibwe, the inhabitants of the neighbouring fourteen villages situated within a 10 km radius of Kibwe, and all patients visiting the Lulingu hospital and the Lwenga dispensary. 1528 persons in the villages and 234 patients in the hospital and dispensary were interviewed and examined (see table). Nearly 40% had no vaccination scars. None had experienced illness with rash during recent months.

INVESTIGATION OF POPULATION IN VICINITY OF MONKEYPOX CASE

—	Population	No. (*% unvaccinated*)			
		Examined	Age (yr)		
			0–4	5–14	≥15
Kibwe village	30	30 (*33*)	9 (*89*)	9 (*0*)	12 (*17*)
Other villages	1498	1103 (*43*)	301 (*67*)	277 (*32*)	525 (*34*)
Hospital and dispensary*	..	234 (*17*)	68 (*47*)	62 (*16*)	104 (*0*)
Total	1528	1367 (*38*)	378 (*64*)	348 (*28*)	641 (*29*)

*Patients seen on the day of the team's visit

Discussion

The natural reservoir of monkeypox virus is not known, and it has not been possible to determine how human beings become infected. Many patients have reported prior contact with monkeys, through the preparation and eating of their flesh; however, because monkeys are frequently eaten in these areas, it has been uncertain whether such contact was significant. The case reported here, however, appears to be especially important.

Since it was not possible to capture the chimpanzee and to determine whether it had been infected, we cannot state with certainty that monkeypox virus was transmitted to the baby as a result of the bite. However, several observations suggest that this was so. First, it has been demonstrated that chimpanzees are susceptible to monkeypox virus and suffer a disease with rash: in 1966, although the disease was noted as mild, chimpanzees were infected in Rotterdam zoo during a monkeypox outbreak in a non-human primate colony;[4] and in 1968 a generalised rash from which monkeypox virus was isolated developed in two chimpanzees shipped from Sierra Leone to a laboratory in Paris.[5] In addition, ten primate serum samples collected in west and central Africa have been shown to contain antibodies specific for monkeypox virus[6] (and J. H. Nakano, personal communication). In this region, more than 30 human monkeypox cases have been discovered during the past ten years. The ten monkeys with monkeypox antibody were *Colobus* spp. and *Cercopithecus* spp. The mother's statement that the chimpanzee was covered with ash-coloured dust and that some hair on the trunk and extremities had been lost suggests the possibility that the chimpanzee had monkeypox infection.

The second finding suggesting transmission of monkeypox virus to the baby by the chimpanzee bite is that the rash appeared 12 days later, a period consistent with the presumed incubation period of human monkeypox (9–19 days) which has been observed in several cases of presumed person-to-person transmission of human monkeypox, although such cases are rare. Thirdly, epidemiological investigation showed no evidence that monkeypox-like disease had occurred in previous months in the immediate area of the case or that the baby had been exposed to any disease with rash during the three weeks before the onset of infection, except the chimpanzee. Moreover, neither the baby nor the family had had recent contact with monkeys other than the chimpanzee.

These findings provide the strongest evidence yet that a wild non-human primate may have been the source of a human monkeypox infection. The question of whether chimpanzees, and other primates, are the primary reservoir of

monkeypox virus or whether there is another lower mammalian reservoir remains to be answered.

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Correspondence should be addressed to I. A., Smallpox Eradication Unit, World Health Organization, 1211 Geneva 27, Switzerland.

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Preliminary Communication

NEUROTENSIN STIMULATES DEFAECATION

JOHN CALAM ROBERT UNWIN
W. STANLEY PEART

Medical Unit, St Mary's Hospital, Praed Street, London W2 1NY

Summary Five normal adults defaecated within 2½ hours of receiving neurotensin 13·5 pmol $kg^{-1}min^{-1}$ for 30 min, whereas none did so after control infusions, in a double-blind study. Neurotensin caused borborygmi and production of stools which resembled the normal contents of the proximal and distal colon in terms of consistency and electrolyte content. This evidence suggests that neurotensin had a major effect on propulsive colonic motility. Blood neurotensin concentrations during infusion were about three times higher than normal postprandial concentrations, but plasma neurotensin is raised in some diseases associated with diarrhoea.

INTRODUCTION

EATING is often followed by defaecation, particularly in certain disease states. The mechanism of this gastrocolic reflex is not known. None of the gut peptides which show a postprandial rise in plasma concentrations lead to defaecation. Neurotensin (NT) is a tridecapeptide which is released from the small intestine by food, and in particular by fat,[1] but its physiological role remains obscure. Three normal individuals defaecated within an hour of receiving NT (12 pmol $kg^{-1}min^{-1}$ for 15 min) and this prompted the double-blind study reported below.

METHODS

The study was approved by the hospital ethics committee. The hospital pharmacy provided coded pairs of vials (control and NT). Control infusions consisted of a vehicle alone. Five healthy men aged 26–34 years received infusions of NT or control on separate days after lunch had been eaten, and after any after-lunch defaecation had occurred. We chose this time of day to minimise the likelihood of defaecation after control infusions. Neurotensin was infused at a rate of 13·5 pmol $kg^{-1}min^{-1}$ for 30 min into an arm vein. Blood was withdrawn for NT assay from a vein in the other arm before, at the midpoint of, and at the end of each infusion. Any symptoms were recorded and any stools passed within 3 h of the infusion were collected. Before and at the end of each infusion the pulse-rate was noted and blood-pressure recorded by means of a standard sphygmomanometer.

Stools were weighed, diluted with an equal weight of distilled water, and homogenised in a Waring blender. A stool sample was retained for estimation of water content and the remainder was centrifuged at 49 000 *g* for 3 h. The supernatant was assayed for sodium and potassium by flame photometry (Corning 430) and for chloride by a potentiometric method (Corning 925). Electrolyte concentrations were expressed in terms of stool water, estimated by drying to a constant weight at 120°C.

NT was measured by radioimmunoassay with antibody L170 at a final titre of 1:500 000. This antibody was donated by Prof. G. J. Dockray and is specific for the C-terminal of NT. Synthetic NT (Cambridge Research Biochemicals) was used as a standard and was also used to make tracer by the chloramine T method.[2] NT was extracted from plasma by 'Sep-pak C18' (Waters) before the radioimmunoassay in which 30 pmol l^{-1} NT produced 50% inhibition of tracer binding. Charcoal coated with dextran and plasma was used to separate free tracer from bound tracer.

RESULTS

None of the men defaecated within 3 h of a control infusion, whereas all five passed stools between 15 and 150 min after the end of NT infusion. Two men experienced mild colic and passed formed stools, two passed a mixture of formed and sloppy material, and one passed only sloppy material. All subjects had borborygmi after NT. The stools had a median weight of 94 g (range 11–258 g) and water content of 78% (72–88%). Sodium and potassium concentrations in stool water were 75 (11–109) mmol l^{-1} and 98 (51–133) mmol l^{-1}, respectively, with sodium/potassium ratios of 0·6/1 (0·1/1–2·1/1). Stool water chloride was 36 (14–63) mmol l^{-1}. Plasma NT-like immunoreactivity was 14 (<14–45) pmol l^{-1} (n=20) before infusions and during control infusions; peak concentration during NT infusions was 540 (370–990) pmol l^{-1} (n=5). Mean blood-pressure was 130/78 mm Hg before and 128/81 mm Hg at the end of NT infusions (NS), and mean heart-rate was 65 beats min^{-1} at both times.

DISCUSSION

The presence of borborygmi after NT suggests that it had a major effect on motility, and the passage of formed stools in two men indicates that propulsive colonic motility occurred. The passage of some sloppy material containing more sodium than potassium suggests that material was ejected from the right colon and it is possible that ileal motility was also increased. Effects on secretion and reabsorption of water or electrolytes cannot be excluded. The only previous in-vivo study of NT and colonic motility was in the anaesthetised cat.[3] Propulsive colonic motility did not occur, but antiperistalsis was stimulated in the proximal colon by a dose of NT per kg similar to that used in the present study. Exposure of guineapig colon to NT in vitro leads to transient relaxation, followed by contraction. This appears to be due to a direct effect of NT on muscle and these effects occur at a concentration of 100 pmol l^{-1}, which is below reported peak postprandial concentrations.[4] The better known contracting effect of NT on ileal muscle requires concentrations about 10 times higher than 100 pmol/l and is probably indirect.[5]

In 1913 Hertz and Newton, using barium follow-through studies, found that eating caused colonic mass peristalsis which led to defaecation.[6] There have been several attempts to determine the mechanism of this response, usually based on the measurement of intracolonic pressure waves after a meal.