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A Second Sooty Mangabey Monkey with Naturally Acquired Leprosy: First Reported Possible Monkey-to-Monkey Transmission[1]

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In 1979 we diagnosed naturally acquired leprosy in a sooty mangabey monkey (*Cercocebus atys*) ([7, 8]). The disease in that mangabey (A015), classified as subpolar lepromatous leprosy (LLs), progressed rapidly, requiring treatment with antileprosy drugs 13 months after diagnosis ([7, 8]).

Extensive studies, including DNA homology, identified the etiologic agent of the disease in A015 as *Mycobacterium leprae* ([8]). More recently the detection of anti-phenolic glycolipid-I antibodies in infected monkeys (Gormus, *et al.*, unpublished data) and mycolic acid analysis (Portaels, *et al.*, personal communication) have provided additional evidence that the causative agent is *M. leprae*. Prior to A015 only one other nonhuman primate, a chimpanzee from Sierra Leone, had been observed with naturally acquired leprosy ([3, 4]).

The discovery of naturally acquired leprosy in a sooty mangabey prompted us in 1980 to undertake experimental transmission studies in mangabeys and three other primate species. The results showed that over 80% of sooty mangabeys inoculated experimentally with *M. leprae* developed leprosy ([15]). Rhesus (*Macaca mulatta*) and African green monkeys (*Cercopithecus aethiops*) also appear to be susceptible, and will be valuable models in experimental leprosy ([15]). Squirrel monkeys (*Saimiri sciureus*) developed no evidence of leprosy after inoculation with *M. leprae* ([15]).

The previous observations showed that mangabey A015 was not a uniquely susceptible individual, but questions remained concerning the likelihood of natural transmission of leprosy between monkeys, or between monkeys and humans.

In September 1986, we obtained a second female sooty mangabey monkey (G932) with clinical and histopathologic characteristics of leprosy. All laboratory examinations thus far performed confirm the identification of the etiologic agent as *M. leprae*. Of particular interest is the history of exposure of this second animal (G932) to the first mangabey with naturally acquired leprosy (A015). It is likely that G932 contracted leprosy by contact with A015; if so, this represents the first reported probable natural monkey-to-monkey transmission of leprosy.

MATERIALS AND METHODS

The animal was sedated with ketamine HCl (5 mg/kg) for clinical examinations and collecting specimens. Biopsy specimens for histopathologic examination were processed by routine methods and stained by hematoxylin-eosin and Fite-Faraco methods. Published procedures were used to test for pyridine extractability of acid fastness and mouse foot pad growth of *M. leprae* ([1, 10]). Lepromin skin testing was performed using 0.1 ml of killed *M. leprae* at 4×10^9 and 8×10^9 bacteria/ml, representing 25 and 50× standard lepromin concentrations.

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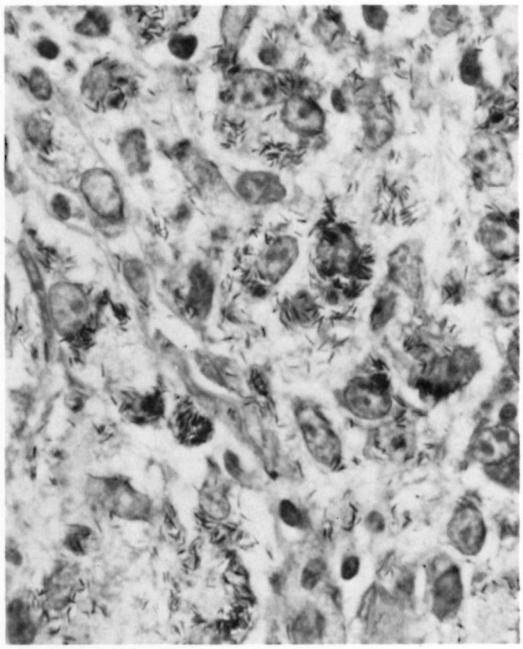

FIG. 1. Mangabey G932. Histologic section of chin lesion showing large numbers of *M. leprae* in histiocytes (×1000). AFIP Neg. 86-10117.

FIG. 2. Mangabey G932 (4 months after diagnosis). Note nodules around eyes and on nose, muzzle, ear, and chin. AFIP Neg. 87-5513.

These concentrations were used because mangabeys require higher doses of lepromin than humans to elicit positive skin test responses (Gormus, *et al.*, unpublished data).

RESULTS

In September 1986, the facial skin of mangabey G932 was heavily infiltrated and thickened, especially on muzzle areas such as the chin, cheeks, nose, and periorbital regions, including the eyebrow area. The margins of both ears were thickened and erythematous. There were no other lesions. Nasal secretions contained large numbers of acid-fast bacteria (AFB). The acid fastness of the organisms was pyridine extractable, and the growth pattern in normal BALB/c mouse foot pads indicated that the organism is *M. leprae* ([1, 10]). A biopsy from the skin of the chin showed extensive infiltration of vacuolated histiocytes that contained large numbers of AFB (Fig. 1). A high percentage of the AFB were solidly stained. Dermal nerves were invaded by cellular infiltrates and AFB, and perineuria were thickened (Fig. 1). These findings are consistent with subpolar lepromatous leprosy (LLs) in humans and are similar to those demonstrated in mangabey A015 in 1979 ([7, 8]).

Mangabey G932 was lepromin skin-test negative in October 1986. Peripheral blood mononuclear cells were tested in December 1986, and again in July 1987, for *in vitro* blastogenic responses to lepromin and to the mitogens phytohemagglutinin (PHA), concanavalin A (ConA), and pokeweed mitogen (PWM), by methods previously reported ([6, 9]). Positive responses were obtained using each of the four stimultants on both dates, but the magnitude of the responses had diminished 50–60% during that time interval. During that 7-month period, the disease had advanced (Figs. 2 and 3) and had become more widespread with ulceration of lesions and severe anemia. Lesions had appeared on the outer lateral surfaces of the feet (Fig. 4), suggesting an unnatural gait that may have resulted from a neuropathy.

Mangabey G932 was pregnant when we received her and a full-term male infant was born 13 October 1986. The infant died one day after birth, and necropsy revealed no gross or microscopic evidence of leprosy. The placenta was not available for study.

DISCUSSION

G932 had previously been housed together with A015 and other sooty manga-

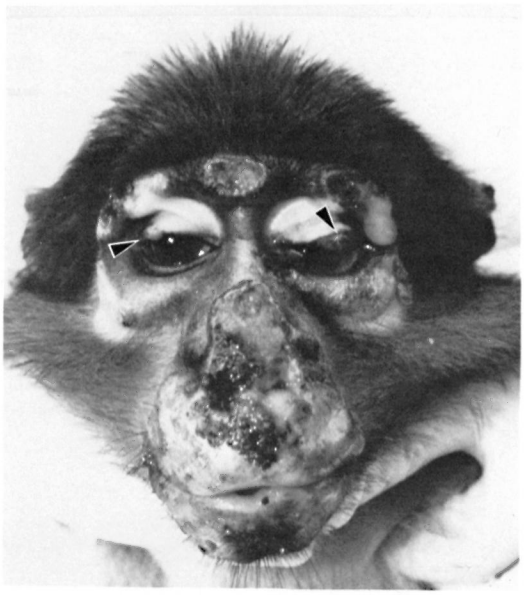

FIG. 3. Mangabey G932 (8 months after diagnosis) with ulceration of nodules on nose and muzzle. Note lepromatous nodules in the eyelids (arrows) and ulceration of lesions that were absent in Fig. 2. DRPRC Neg.

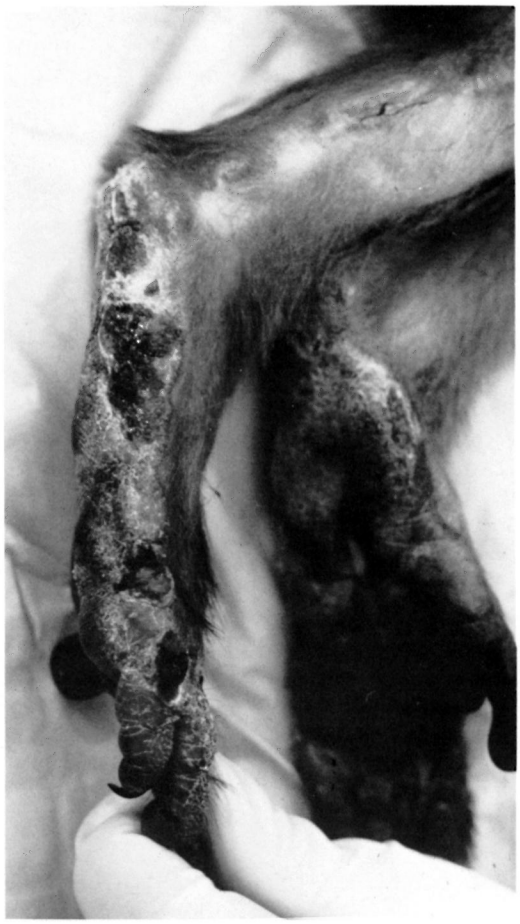

FIG. 4. Mangabey G932 (8 months after diagnosis) with ulceration on outer surface of right foot. Note dry, scaly appearance of the skin, especially on the toes. DRPRC Neg.

beys at the Gulf South Research Institute (GSRI), New Iberia, Louisiana, U.S.A. (now the University of Southwestern Louisiana-New Iberia Research Center) in a cage that permitted free direct physical contact among the animals. A015 was removed from this caging facility and transferred to the Delta Regional Primate Research Center (DRPRC) Covington, Louisiana, U.S.A., in December 1979 after she developed leprosy ([7, 8]). G932 remained at GSRI until her transfer to the DRPRC after the appearance of the described lesions during the summer of 1986.

Both A015 and G932 were imported separately to the GSRI from Nigeria with other sooty mangabeys in January 1976, where they remained in direct contact with each other until 1979. Neither animal was experimentally exposed to infectious agents.

A015 developed clinically apparent leprosy in 1979. G932 showed no signs of leprosy until skin lesions appeared in 1986, suggesting that G932 contracted leprosy from A015. This is the first reported instance of probable transmission of leprosy from monkey to monkey. A015 may have contracted leprosy from contact with an infected human or mangabey or by other means. The history of both animals prior to their shipment from Nigeria is unknown, precluding any definitive conclusions concerning the ultimate origin of their disease. Without such knowledge, it remains possible that both A015 and G932 could have contracted leprosy by exposure to a third common source or to independent sources of *M. leprae* infection. The *M. leprae* isolated from A015 was partially resistant to dietary dapsone when tested in BALB/c mouse foot pads (inhibited by 0.01%, but only partially inhibited by 0.001% and 0.0001%) ([8]). This partial dapsone resistance suggests that the source of the *M. leprae* was a leprosy patient who received irregular dapsone therapy. The dapsone sensitivity of the isolate from G932 is presently being tested.

The discovery of a second sooty mangabey with naturally acquired leprosy provides strong support for the suggestion that leprosy is a zoonotic disease in this primate species ([13]). Naturally acquired leprosy is common among armadillos ([12–14]) and has been observed in a chimpanzee ([3, 4]). The importance of zoonotic leprosy in the epidemiology of the human disease is unknown, but increasing evidence suggests that humans can acquire leprosy by contact with diseased armadillos and that it is a significant risk factor in indigenous leprosy in the U.S.A. ([2, 5, 11]). The data presented in this report suggest that mangabeys may be a reservoir for *M. leprae* in leprosy-endemic areas of Africa inhabited by these monkeys. Information from additional mangabeys will be required to confirm this possibility, and to determine the extent of naturally acquired leprosy in this primate species in their natural habitat. Further study is especially warranted because mangabeys, usually quite friendly and sociable, are often kept as pets and used as food in Africa.

SUMMARY

The existence of naturally acquired leprosy in a second sooty mangabey monkey has been documented. The disease has the clinical and histopathological characteristics of subpolar lepromatous leprosy (LLs), and microbiological studies thus far confirm the etiologic agent as *Mycobacterium leprae*. This mangabey had been housed in direct contact with the first mangabey in which naturally acquired leprosy was diagnosed in 1979. Clinical symptoms appeared in the second mangabey in 1986, almost 7 years after the appearance of skin lesions in the first monkey. It is likely that the second mangabey contracted leprosy from the first mangabey or that both animals contracted the disease by contact with an unknown common third source. This is the only known possible natural transmission of leprosy from monkey to monkey, and suggests that a potential zoonosis exists in wild monkeys that may serve as a reservoir for the disease in areas where human leprosy is endemic.

RESUMEN

Se describe un caso de lepra natural en un segundo mono mangabey "tiznado". La enfermedad tiene las características clínicas e histopatológicas de la lepra lepromatosa subpolar (LLs) y los estudios microbiológicos realizados hasta ahora confirman que el agente etiológico es *Mycobacterium leprae*. Este mono mangabey había sido alojado en contacto directo con el primer mangabey en el cual se diagnosticó lepra "natural" en 1979. Los síntomas clínicos aparecieron en el segundo mono mangabey en 1986, casi 7 años después de la aparición de lesiones en la piel del primer mono. Es probable que el mangabey segundo se contagió y resultó con lepra por medio del primero, o tambien, los dos se infectarion par un medio común y desconocido. Este es el único caso conocido de la posible transmisión natural de la lepra de mono a mono y el hallazgo sugiere que en los monos salvajes existe una zoonosis potencial donde los monos pueden servir como reservorios de la enfermedad en las áreas endémicas de la lepra.

RÉSUMÉ

L'existence d'une lèpre acquise naturellement dans un deuxième singe mangabey a été étudié. La maladie a présenté les caractéristiques cliniques et histopathologiques d'une lèpre lépromateuse sous-polaire (LLS); les études microbiologiques menées jusqu'à présent confirment que l'agent étiologique est *Mycobacterium leprae*. Ce singe mangabey avait été élevé en contact direct avec la premier singe mangabey chez lequel une lèpre acquise naturellement avait été diagnostiquée en 1979. Les symptômes cliniques sont apparus chez le second singe en 1986, près de 7 ans aprés l'apparition de lésions cutanées chez le premier singe. C'est probable ce le deuxième singe mangabey acquise le lépre de le premier singe mangabey, or tous les deux animals acquise le lèpre sur contact avec une inconnue commune troisième source. Ceci est le seul cas connu de transmission possible naturelle de la lèpre de singe à singe. Cette observation suggère l'existence possible d'une zoonose chez les singes sauvages, qui pourraient ainsi servir de réservoir pour la maladie dans des régions où la lèpre humaine est endémique.

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