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Spontaneous Nocardial Brain Abscess in a Juvenile Rhesus Macaque (*Macaca mulatta*)

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Abstract

Background—A juvenile rhesus macaque presented with blindness, ataxia, and head tilt.

Methods—Postmortem gross and microscopic examination, histochemical staining and bacterial culture were performed.

Results—*Nocardia* sp. was identified as the etiologic agent of a primary pneumonia with secondary cerebral abscessation.

Conclusions—Nocardiosis should be a differential diagnosis for patients with neurologic disease.

Keywords

Nocardiosis; *Nocardia* spp.; monkey; nonhuman primate

Introduction

Nocardia spp. are aerobic gram-positive saprophytic bacteria reported to cause disease in humans [9], and many animal species [1]. Reported cases of nocardiosis in nonhuman primates are few. The most recently published case occurred in a gorilla at the Calgary Zoo which developed spinal abscesses attributed to *N. asteroides* [2]. A small number of cases of disseminated [3,4] as well as localized[5–8] infection in nonhuman primates have been described previously, yet published cases of cerebral nocardiosis are rare [10, 11]. This is in contrast to the larger collection of published human cases which indicate that *Nocardia* spp. have a preference for the cerebrum [5, 7], and account for two percent of all brain abscesses [5]. Previously thought to be an opportunistic infection of immunocompromised populations, nocardial encephalitis has been increasingly reported among immunocompetent patients in recent years [3, 6].

In this case report, we describe the clinical presentation and subsequent pathologic findings of a case of pulmonary nocardiosis with secondary meningoencephalitis.

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Case Report

A one year old female Indian-origin rhesus macaque (weight= 2.5 kg) was born and housed at the AAALAC-accredited Oregon National Primate Research Center (ONPRC), in an outdoor breeding group while assigned to a colony breeding protocol approved by the ONPRC Institutional Animal Care and Use Committee. The patient was serologically negative for simian retrovirus type D and *Macacine herpesvirus* 1. She was fed LabDiet 5000 (PMI Nutrition International, LLC, Brentwood, MO) twice daily and supplemental produce or other enrichment once daily, and water was available *ad libitum*.

In December of 2010, the macaque was admitted to the colony hospital for signs of blindness while in her social group. On presentation, her demeanor was quiet and she sat on the bottom of the cage staring blankly. A slight right-sided head tilt and bilateral mydriasis were noted. She was sedated for further examination with ketamine hydrochloride (10 mg/kg; Ketathesia™, 100 mg/mL, Butler Animal Health Supply, Dublin, OH) intramuscularly. There were no signs of obvious trauma. Her temperature was 102.2°F. Signs of diarrhea were observed, and fecal parasitology screen and culture were collected. Results of a handheld blood analyzer evaluation (i-Stat® Portable Clinical Analyzer, Abbott Point of Care Inc., East Windsor, NJ) and fluorescein staining were within normal limits. Hematology results demonstrated a mild leukocytosis ($21.6 \times 10^3/\mu\text{L}$), characterized by a moderate mature neutrophilia ($17.5 \times 10^3/\mu\text{L}$), a mild monocytosis ($1.1 \times 10^3/\mu\text{L}$), and a mild basophilia ($0.3 \times 10^3/\mu\text{L}$). All remaining values were within the reference intervals established at the ONPRC for healthy rhesus macaques.

Meningitis, blunt head trauma, cerebral abscess, and cerebral neoplasia were included in the differential diagnosis of the neurologic deficiencies observed. Treatment with enrofloxacin (25 mg IV; Baytril™ 100mg/ml, Bayer, Shawnee Mission, Kansas) and mannitol (3.2g IV; mannitol injection 20%, Phoenix™, Clipper Distributing Company, LLC, St. Joseph, MO) were initiated, while the patient received intravenous fluid therapy (225ml Norm-R). Over the course of the day, her appetite was normal, though when returned to her hospital cage, she preferred to stay at the top of the cage and circle to the right. Episodes of atypical behavior characterized by abnormal posture and unresponsiveness to observers for several minutes developed 24 hours after admission. Over the next two hours, tonic-clonic seizures of short duration developed at which time she was euthanized.

Examination of the brain at necropsy revealed a diffusely swollen and pale cerebrum. Distorting the sulcus lunatus of the left hemisphere and extensively involving the occipital lobe and a portion of the parietal lobe was a poorly delineated, raised, irregular focus of pallor. A similar, although less severe, lesion was present in the right frontal lobe, involving the precentral gyrus.

On coronal section, the affected areas were cavitated and filled with abundant, highly viscous green-gray material (Fig.1.) Additional necropsy findings included a $0.5 \times 0.5 \times 1.0 \text{ cm}^3$ area of brown fibrous consolidation in the right cranial lung lobe margin. There was a modest amount of thymic tissue, estimated at approximately 50 to 75 % expected volume for age. The mesenteric lymph nodes were enlarged, firm, and uniformly off-white.

Histological examination of the brain revealed extensive areas of chronic-active, necrotizing pyogranulomatous inflammation characterized by cavitation, central necrosis containing neutrophils and abundant cellular debris, and dense circumferential infiltrates of multinucleated giant cells and epithelioid macrophages (Fig. 2.) Large numbers of multinucleated giant cells, macrophages, and fewer lymphocytes, eosinophils, neutrophils and fibroblasts populated the adjacent parenchyma. Inflammatory infiltrates and necrotic debris also expanded the leptomeninges. These foci were present in the cerebrum, and in a brainstem lesion that was not apparent grossly. Similar histologic findings were present in the lung, in addition to pleural fibrosis, as well as in the mesenteric lymph node. Tangles of slender, argyrophilic branching bacteria were identified predominately at lesion margins in the brain, lung and mesenteric lymph node using Grocott's Methenamine silver nitrate method (Fig. 2.) These organisms were also visible in tissue with Coates Modified Fite acid-fast stain. Weakly Gram-positive filamentous bacteria were isolated on aerobic culture of the cerebral exudate and were identified as *Nocardia*. Speciation was not performed.

Discussion

Nocardia sp. infection occurs by one of three main routes: inhalation, trauma, or ingestion [1]. Given the pulmonary lesion identified at necropsy and the chronicity of the inflammation present when compared to that of the cerebrum and brainstem, the most likely route of infection was inhalation. In one report of a nocardial brain abscess in a cynomolgus macaque, the authors remarked that the monkey had never lived outdoors, and thus had no opportunity for exposure to potentially contaminated soil [11]. Although the monkey in our case report did live her entire life outdoors in sheltered housing, the floor of the structure is concrete, which decreases the likelihood of direct contact with decayed organic material. Presumably, exposure occurred via inhalation of contaminated dust.

No other animals within the social group developed clinical signs attributable to nocardiosis (i.e. pneumonia or encephalitis). *Nocardia* is an exceedingly rare pathogen in our facility. Review of pathology records spanning a 47 year period revealed only three other cases: one case of abdominal lymphadenitis and two cases of necrotizing pneumonia from animals in quarantine. All three cases occurred in rhesus macaques and the most recent case occurred in 1977. Because of the isolated nature of the illness, no environmental sampling was performed to identify the source of the infection.

Antimicrobial therapy was initiated in this case; however, nocardial infection was not suspected and consequently was not targeted. Cases of nocardial brain abscess in humans are often treated with a combination of antimicrobials, as well as surgery to evacuate the abscess and obtain biopsy and culture samples [7, 8]. Though sulfonamides are the first choice for therapy in humans [5, 7, 8], there have not been any successful reports of *Nocardia* treatment in nonhuman primates [4].

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Figure 1. Coronal brain sections showing an abscess in the left (L) parietal lobe (A) and left (L) occipital lobe (B). Bar = 1cm.

Figure 2.

Abscess within the occipital lobe. Arrows indicate margin of abscess. (A), H&E, (Bar =500 μ m); Grocott's Methenamine silver nitrate method illustrating filamentous branching bacteria (B) (Bar = 50 μ m); Acid-fast bacteria (arrow) with Coates Modified Fite stain for Nocardia (C) (Bar = 50 μ m); impression smear (D) of the abscess showing weakly Gram-positive filamentous bacteria (arrow) (Bar = 50 μ m).