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Septicemia in an Indian Rhesus Macaque (*Macaca mulatta*) associated with *Providencia stuartii*

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Abstract

Providencia stuartii (*P. stuartii*) is an opportunistic pathogen and major concern in urinary-catheter-related infections in human medicine. Here we report *P. stuartii* induced septicemia in an eighteen-year-old, female India-origin Rhesus macaque with multiple traumatic wounds. The animal had neutrophilic leukocytosis, necrosuppurative meningoencephalitis, hypophysitis and bronchopneumonia with vasculitis, thrombosis, and clusters of extracellular Gram-negative bacilli. *P. stuartii* was isolated from the lesions of the brain and lung and confirmed by PCR and sequencing. To the authors' knowledge, this is the first case of septicemia associated with *P. stuartii* in a nonhuman primate.

Keywords

Providencia stuartii; septicemia; rhesus macaque

Providencia stuartii (*P. stuartii*) is a Gram-negative bacterium that is commonly found in soil, water, and sewage.[6] It is an opportunistic pathogen commonly seen in patients with purple urine bag syndrome associated with severe burns or long-term indwelling urinary catheters. [5, 17] Occasionally *P. stuartii* has also been associated with bacteremia [18], diarrhea [19], peritonitis [15], meningitis [13], infections of burn wounds [8], endocarditis [4, 12], renal abscesses [1], and septicemia [3] in humans. Infections with *P. stuartii* are rarely documented in animals, but it has been linked to neonatal diarrhea in dairy cows [16], and ulcerative dermatitis and cellulitis in a canine [9]. Here, we report a case of septicemia associated with *P. stuartii* infection in a nonhuman primate.

An 18-year-old, female India-origin Rhesus macaque (*Macaca mulatta*) presented with multiple traumatic skin wounds, obtunding, lethargy and increased respiratory sounds from the outdoor breeding colony at the Tulane National Primate Research Center (Covington, Louisiana). Hematology showed a moderate neutrophilic leukocytosis (total white blood cell count was 15,690/ μ l with 72.1% neutrophils, reference range 20.6 - 46.9%). Radiographs

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remained inconclusive. Euthanasia was elected due to the lack of responsiveness to antibiotic treatment and deteriorating physical condition.

Grossly the lung lobes were irregularly collapsed with a cobblestone appearance (Fig. 1a). The elevated areas were pale-white and often associated with small (3-5 mm) to large (3-5 cm) emphysematous bullae. Other areas were purple and depressed. On the cut surfaces the dilated bronchioles contained variable amount of suppurative exudate. The bronchial lymph nodes were markedly enlarged. The meninges of the brain were diffusely opaque and hemorrhagic. There was an abscess in the left parietal lobe, accompanied by a large accumulation of grayish-yellow fibrinopurulent meningeal exudate (Fig. 1b). All other organs were grossly unremarkable.

Microscopically 50% to 60% of the pulmonary architecture was obliterated by large amount of edema and fibrin, numerous degenerate neutrophils and erythrocytes, and fewer macrophages, lymphocytes and plasma cells (Fig. 2a). Scattered in this area, there were many, variably-sized emphysematous alveoli. In the less affected areas, the alveoli contained small to moderate amounts of exudate. Bronchi and bronchioles were ectatic and contained moderate amounts of exudate. They were lined by either attenuated or hypertrophied and hyperplastic ciliated and secretory cells. The walls of bronchi, bronchioles, blood vessels, and pleura were moderately to severely expanded by edema, fibrin, and small numbers of inflammatory cells. Bronchial lymph nodes were enlarged by edema, hemorrhage, and dilated sinuses. The meninges of brain and spinal cord were diffusely expanded by edema, fibrin, numerous degenerate neutrophils, and many erythrocytes (Fig. 2b). Multifocal mild vasculitis and perivasculitis were noted in the neuropil of the brain and spinal cord. The pituitary gland, especially the pars nervosa, was effaced by abscesses. Diffusely there was mild, acute, purulent peritonitis. Mild, chronic hepatitis was noted, but there was no discrete abscess formation in the liver or other organs. Clusters of Gram-negative bacteria were observed in the lungs and meninges (Fig. 2b Inset). *Providencia stuartii* was cultured from the brain and lung. For etiology confirmation, we extracted DNA from brain and lung tissues using DNeasy Blood & tissue kit (Qiagen) and performed PCR using universal bacterial forward primer (5'-AGAGTTTGATCMTGGCTCAG-3') and reverse primer (5'-AAGGAGGTGWTCCARCC-3') to amplify 16S rRNA bacterial gene. The ~1500bp PCR product was purified using DNA clean & concentration kit (Zymo research) and used for sequencing to confirm a definitive *Providencia stuartii*. A total of 208 bases were queried in NCBI BLAST search and yielded a 92% nucleic acid identity match with the *Providencia stuartii* ATCC 29914 (taxid: 588).

Since *Providencia* sp. was first isolated from chickens thought to be infected with fowl cholera in 1904, the bacteria in the genus *Providencia* have had many taxonomical changes and are still frequently confused with other organisms in the genera *Proteus* and *Morganella*. [6, 7] Currently genus *Providencia* has 5 species, including *P. stuartii*, *P. rettgeri*, *P. alcalifaciens*, *P. rustigianii*, and *P. heimbachae*. [7]

Although *P. stuartii* infections are rare, it has long been recognized as a pathogen for nursing home patients with chronic indwelling urinary catheters. *P. stuartii* was one of the most common bacteria isolated from patients with purple urine bag syndrome. [5] Upwards of

61% of urinary tract specimens in these patients contain either *P. stuartii* or *Proteus mirabilis*. [17] The persistence of bacteria in the urinary tract is likely due to an adhesin, mannose-resistant/*Klebsiella*-like hemagglutinin, which allows bacteria to adhere to urinary catheters. [2, 10] *P. stuartii* has also been linked to bacteremia [18], diarrhea [19], peritonitis [15], infections of burn wounds [8], endocarditis [4, 12], renal abscesses [1], and septicemia [3] in humans. Recently 3 cases of *P. stuartii* meningitis have been documented and presumed to be nosocomial infection in human medicine. [11, 13, 14] The source of *P. stuartii* infection in our case is unknown, but nosocomial infection did not fit the clinical history. Given that *P. stuartii* is commonly found in soil, water, and sewage [6] and our patient had multiple concurrent skin traumas, contamination of a skin wound is likely.

Although *P. stuartii* is one of most common bacteria in the environment, the occurrence of *P. stuartii* infection is rarely reported in the veterinary literature. To the authors' knowledge, there are no reported cases of *P. stuartii* infection in nonhuman primates.

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Figure 1.

a: Necrosuppurative bronchopneumonia, Indian rhesus macaque. All lung lobes were irregularly collapsed with a cobblestone appearance characterized by bronchial and bronchiolar ectasis and atelectasis. A large bulla in left anterior lobe (arrow) and numerous emphysematous bullae in all lung lobes were noted. b: Necrosuppurative meningitis, Indian rhesus macaque. Meningeal hemorrhages associated with a large abscess of the left parietal lobe.

Figure 2.

a: Histopathology of lung, Indian rhesus macaque. Necrosuppurative bronchopneumonia with bronchial ectasis (*), atelectasis and perivascular edema (+) dominate most low power microscopic fields. HE, 20X. Inset, fibrin, edema and numerous degenerate neutrophils. Magnification 400X. b: Histopathology of brain and meninges, Indian rhesus macaque. Necrosuppurative meningoencephalitis with clusters of bacilli. H&E. Magnification 50X. Inset, meninges, Gram (-) bacilli. Magnification 1,000X.