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Air sacculitis in three rhesus macaques (*Macaca mulatta*) and one Japanese macaque (*M. fuscata*)

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Abstract

Bacterial infection of the laryngeal air sacs (air sacculitis) is infrequently reported in nonhuman primates, where it leads to chronic respiratory disease. It is particularly uncommon in macaques; however, we report here suppurative air sacculitis with extension to adjacent cervical tissues in three rhesus and one Japanese macaque. *Staphylococcus aureus*, *Streptococcus* sp. and an anaerobic bacterium were isolated.

Keywords

Nonhuman primate; laryngeal air sac; monkey; cervical abscess

Introduction

Air sacculitis, often a chronic subclinical infection in nonhuman primates, is frequently associated with gram-negative or mixed bacterial infections [4]. It is infrequently reported in the literature, with a 0.7% incidence in baboons reported at necropsy in one facility [4]. Orangutans seem especially susceptible and experience more severe disease [5,9]. Other species in which air sacculitis has been identified include owl monkeys, pig-tailed macaques, chimpanzees, bonobos, and gorillas [4,6].

Functions ascribed to air sacs in nonhuman primates include vocal modulation, involvement with sexual and aggressive behaviors, and buoyancy during swimming [4,5,9]. Air sacs in macaques are not as well-developed as those in other species such as orangutans [4,9], siamangs [6], baboons [5], and New World monkeys [3]; but their presence may continue to serve some function in vocalization [7,8]. In the rhesus, they are comprised of a thin membrane arising from the caudal epiglottis and lying between the ventral thyroid cartilage and hyoid bone [2]. This report describes the first cases of air sacculitis in rhesus and Japanese macaques.

Case report

A 14 year-old male Japanese macaque was housed outdoors in a one-acre corral and exhibited no clinical signs prior to euthanasia at study endpoint. At necropsy, the laryngeal

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air sac mucosa was thickened and opaque, and the air sacs were distended with approximately 15 mL of opaque green-tinged white fluid on the left side and 4 mL on the right side (Figure 1). In addition, the tracheal mucosa was thickened, and there was scant cloudy fluid in the tracheal lumen. The diagnosis of air sacculitis in this Japanese macaque prompted a search of the electronic medical record system at the Oregon National Primate Research Center (ONPRC) for cases in which air sacculitis or cervical abscess were found at necropsy. Three additional cases were identified in rhesus macaques. All procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at the ONPRC. The ONPRC is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care, International.

Three indoor-housed adult female rhesus macaques, ranging in age from 11–19 years, presented for acute respiratory signs preceded by a brief period of partial anorexia and depression. Clinical signs (Table 1) included dyspnea accompanied by stertor (n=2), stridor (n=1), and hypoxemia (n=2), in addition to dehydration and weight loss (n=2). On physical examination, marked cervical swelling was present in all cases corresponding to cranial cervical abscessation extending from the caudal aspect of the cheek pouch and pharynx. Due to the poor prognosis associated with the acute, severe clinical presentations of these animals, euthanasia was performed and they were submitted for necropsy prior to additional diagnostics. On gross postmortem examination, none of the animals had external evidence of penetrating trauma which could have contributed to the development of air sacculitis and abscessation. In the rhesus macaques, cervical abscesses measured up to 13 cm in greatest dimension and contained a copious volume of green-to-brown purulent exudate. The surrounding tissues of the pharynx, intermandibular space, submandibular lymph nodes, and subcutaneous tissues were variably edematous and necrotic, with effacement of the normal cervical architecture. Additionally, one animal had developed secondary acute aspiration pneumonia at the time of necropsy. In the Japanese macaque, involvement was limited to the air sac and adjacent trachea (Figure 1).

Bacterial culture was performed in all cases. *Staphylococcus aureus* was isolated in two of four cases, while *Streptococcus* sp. and an anaerobic bacterium were isolated in the remaining two cases (Table 1).

Tissues were routinely processed, sectioned at five microns and stained with hematoxylin and eosin (H&E). In the rhesus macaques, abscesses and extensive necrosuppurative inflammation effaced the walls of the air sacs and extended into the adjacent tissues with accompanying edema. In the Japanese macaque with milder disease, the opacity of the air sac was due to infiltrating plasma cells, lymphocytes and fewer neutrophils and mucosal hyperplasia. There was multifocal degeneration and erosion of the superficial epithelium and a luminal exudate (Figure 1).

Discussion

These four cases occurred over a ten-year period (2005–2014) at the ONPRC. Given an average annual census of 4741 rhesus macaques and 415 Japanese macaques, the incidence of clinical air sacculitis in both species is <0.01%. Clinical signs associated with air

sacculitis in nonhuman primates include lethargy and anorexia, cervical swelling, and intermittent upper respiratory signs [6,9]. In the cases described here, these signs were present in affected rhesus macaques. However, in the affected Japanese macaque, air sacculitis was an incidental finding at necropsy and is thought to reflect an earlier stage of disease.

Three adult rhesus females and one adult male Japanese macaque were identified with air sacculitis in this case series. The apparent gender predilection may reflect the small number of cases identified and/or the relative ratio of females to males in the rhesus colony (3:2). Previous surveys of this condition in nonhuman primates identified an increased incidence of infection in male baboons. Sex predilection was not observed in chimpanzees or orangutans [4,5].

The absence of external traumatic wounds in these cases and those previously reported in other species suggests that infection arises elsewhere. As proposed in other nonhuman primates, the point of entry for bacterial air sacculitis is likely the oropharynx with extension to the cheek pouch or air sacs. Abscessation and subsequent spread through the subcutaneous tissues and possible development of secondary bacterial pneumonia lead to the associated clinical signs [4,9]. An upper respiratory infection or initial mechanical insult may contribute to this initial infection, with drainage into the oropharynx [1]. This proposed pathogenesis is further supported by the isolation of normal upper respiratory inhabitants in the ONPRC cases. Mixed populations of enteric bacteria are most commonly reported in other primates; these may reflect secondary opportunistic pathogens in chronic cases [4,5,9]. Dyspnea in the rhesus macaques reflected acute partial upper airway obstruction by the mass effect of the extensive cervical swelling. Despite the apparent acute onset of the clinical signs, necropsy findings were consistent with a chronic infection and highlight the difficulty of identifying diseases with insidious onset in this population.

This report describes the first cases of air sacculitis in rhesus and Japanese macaques. In the absence of trauma, air sacculitis should be included in the differential diagnosis for animals presenting with cervical swelling, abscessation, or upper respiratory disease with concurrent dyspnea. This would allow increased recognition during clinical assessment and potentially facilitate medical management of this disease, thus minimizing the need for immediate euthanasia.

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Figure 1.

Air sacculitis in macaques. (A) Rhesus macaque, case 3. Cervical swelling extends to thoracic inlet. (B) Rhesus macaque, case 3. Purulent exudate fills the ventral neck area. The adjacent tissues are pale and edematous. (C) Japanese macaque, case 1. Skin and cheek pouch (star) are reflected to reveal thickened air sacs containing a thin exudate (arrow). (D) Japanese macaque, case 1. Air sac margins are extended (arrows), highlighting the opacity of the walls. (E) Rhesus macaque. Normal air sac is lined by ciliated pseudostratified columnar epithelium. H&E, bar = 50 µm. (F) Japanese macaque, case 1. There is epithelial degeneration and erosion with segmental loss of cilia, marked infiltration of plasma cells, lymphocytes and fewer neutrophils in the subjacent tissue, and a luminal exudate of neutrophils admixed with fibrin and necrotic cellular debris. H&E, bar = 50 µm.

Table 1
Signalment, Clinical Signs, Gross Findings and Culture Results of Affected Macaques

Case Number	Species	Age (in years)	Sex	Clinical signs	Relevant gross findings	Culture results
1	<i>M. fuscata</i>	14	M	None	Purulent exudate within air sacs, edema of larynx and epiglottis	<i>Staphylococcus aureus</i>
2	<i>M. mulatta</i>	11	F	Dyspnea, stertor, hypoxemia, cervical swelling, halitosis	Cervical abscess, purulent nasopharyngeal exudate, subcutaneous and pharyngeal edema, tracheitis	<i>Staphylococcus aureus</i>
3	<i>M. mulatta</i>	14	F	Anorexia, depression, dehydration, dyspnea, cervical swelling	Cervical abscess, purulent exudate in left cheek pouch and air sac, subcutaneous edema, submandibular lymphadenomegaly	Alpha-hemolytic <i>Streptococcus</i> sp.
4	<i>M. mulatta</i>	19	F	Anorexia, depression, dehydration, dyspnea, stertor, hypoxemia, cervical swelling, nasal discharge, rales	Cervical abscess, purulent nasopharyngeal exudate, edema of epiglottis and subcutaneous tissues, submandibular lymphadenomegaly and edema, aspiration pneumonia	Anaerobic bacterium (not further identified)