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Case report

Massive attack of honeybee on macaws (*Ara ararauna* and *Ara chloropterus*) in Brazil – A case report

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ABSTRACT

Three adult birds of the species *Ara chloropterus* and five of the species *Ara ararauna* from a conservation breeding facility suffered a massive attack by honeybees. The *A. chloropterus* birds presented swollen puncture lesions with stingers (mainly in the facial regions without feathers), swelling of the eyelids and subcutaneous tissue, and respiratory distress, and they were treated with intramuscular injections of 1.67 mg/kg of promethazine and 10 mg/kg of hydrocortisone followed by removal of the stingers. Complete remission of the clinical signs occurred 48 hours after start of treatment. The five *A. ararauna* birds died before they arrived at the veterinary hospital, and the necropsies found stingers in the areas of the face without feathers and the subcutaneous tissue, which were associated with erythema, bruising, and swelling. Food content from the crop was found in the oral cavity and the tracheal lumen, and marked congestion was observed in the heart, liver, spleen, lungs, kidneys, brain, and cerebellum. Among the histopathological findings, significant swelling of the myocytes in the endocardium and vascular dilation with erythroid repletion were observed, and there were multifocal areas of centrilobular necrosis associated with severe congestion and hemorrhaging in the hepatic tissue. Severe acute tubular necrosis and hydropic-vacuolar degeneration were observed in the kidneys. The clinical signs and pathological findings suggest envenomation due to a massive bee attack, the first such report for Psittacidae.

1. Introduction

Brazil may be considered the cradle of the hybrid Africanized honeybee since African bees (*Apis mellifera scutellata*) imported in the 1950s were cross-bred with European species (*Apis mellifera* and *Apis mellifera ligustica*). The crossbreeding resulted in a bee that produces more honey than the African bee but displays more aggressive behavior than the European species, and this has led to various types of accidents with severe and even fatal results for both animals and humans (Almeida et al., 2011; Clarke et al., 2002; Ferreira et al., 2012; Funayama et al., 2012). This hybrid spread quickly throughout South America, mainly due to the high reproductive rate and migratory behavior of the species, which has increased the number of accidents involving bees (Ferreira et al., 2012).

The toxic effect of bee venom is usually associated with allergic reactions, but massive attacks can be lethal due to the large amount of venom collectively injected into the victim. Bee venom is composed of various allergenic and pharmacologically active substances, including melittin (50–60% of the venom dry weight) and phospholipase A2 (PA2) (11%–12% of the venom dry weight) (Brochetto-Braga et al., 2006). Other substances are present in smaller quantities but play an important role in the toxicity of the venom, including apamin (2% of the venom dry weight), peptide 401 (1–2% of the venom dry weight), hyaluronidase (2% of the venom dry weight), histamine, dopamine, adrenaline, norepinephrine, and serotonin appear in lesser amounts, but play an important role in the toxicity of venom (Han et al., 2000).

Among the birds belonging to the family Psittacidae, nine

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species are currently classified as members of the genus *Ara* (Clements et al., 2013), including the blue-and-yellow (*A. ararauna*) and red-and-green macaws (*A. chloropterus*), both of which are frugivorous and relatively large with long lifespans (Sick, 2001). *A. ararauna* is found in tropical regions in Central America, Brazil, Bolivia and Paraguay, where it inhabits floodplains with buriti palm groves, swamps, savannas and wetlands (IUCN, 2016; Jupter and Parr, 1998; Sick, 2001). *A. chloropterus* is found in Brazil and other South American countries in forested and dry terrain (Jupter and Parr, 1998; Sick, 2001). The two species are already extinct in some regions, while their populations are declining due to shrinking habitat, hunting, and illegal wildlife trafficking in others (IUCN, 2016; Jupter and Parr, 1998).

This article describes a case of a massive attack by Africanized honeybees with a focus on the clinical and pathological aspects of three and five specimens of *A. chloropterus* and *A. ararauna*, respectively.

2. Case report

Three adult birds of the species *A. chloropterus* (mean weight of 1.5 kg) and five adults of the species *A. ararauna* (mean weight of 1.3 kg) were treated at the Wildlife Medicine and Research Center (Centro de Medicina e Pesquisa em Animais Selvagens – CEMPAS) at the School of Veterinary Medicine and Animal Science (Faculdade de Medicina Veterinária e Zootecnica – FMVZ – UNESP) in Botucatu, São Paulo, Brazil after suffering a massive attack by honeybees.

The birds were from a conservation breeding facility located in the state of São Paulo, where they lived in 4-foot by 6-foot outdoor enclosures surrounded by a screen of 2-inch galvanized wire. There was no history of recent diseases or veterinary procedures, so the diagnosis was based on the description of the attack, the observation of stingers during the clinical examination, and lesions consistent with toxicosis caused by bee venom during the necropsy.

The *A. chloropterus* birds presented swollen puncture lesions with stingers (mainly in the facial regions without feathers), swelling of the eyelids and subcutaneous tissue, and respiratory distress. They were treated with 1.67 mg/kg of promethazine (Pamergan®) and 10 mg/kg of hydrocortisone (Ariscorten®) by IM injection followed by removal of the stingers (an average of 45 stings/bird). Approximately ten hours after receiving medication, the birds showed alleviation of the respiratory distress, and they could feed and drink water normally the following day. Two days after the start of treatment, the birds showed no clinical signs and were discharged from veterinary care.

The five *A. ararauna* birds were dead on arrival at the veterinary hospital and were sent to the Laboratory of Ornithopathology (FMVZ/São Paulo State University – UNESP) for necropsy, and the pathological changes observed during the procedure were similar among all the examined birds (Fig. 1A). The external examination found a large number of stingers (an average of 63 per bird) located mainly in the non-feathered areas of the face that were associated with erythema and edema, and food content from the crop was found in the oral cavity and the tracheal lumen (Fig. 1B).

Examination of the subcutaneous tissue showed multifocal hematomas associated with the insertion of stingers and diffuse hematomas, and exposure of the coelomic cavity revealed marked congestion in the heart, liver, spleen, lungs, and kidneys. Moreover, hemorrhagic enteritis was observed, and when the skull cap was removed, congestion was observed in the brain and cerebellum (Fig. 1C).

Lung, heart, liver, kidney, skeletal muscle, and brain tissue samples were fixed in 10% formalin, embedded in paraffin, and processed for hematoxylin-eosin staining.

The lungs of all the birds (5/5) displayed swelling, congestion, and severe bleeding. Three birds (3/5) were found to have a large quantity of aspirated food in the lungs as well as moderate infiltrate composed of heterophils, lymphocytes, and eosinophils (Fig. 1D).

The cardiac muscle tissue of all birds (5/5) showed significant swelling of the myocytes, mainly in the endocardium, and vascular dilation with erythroid repletion resulting in diffuse congestion. The hepatic tissue of three birds (3/5) showed multifocal areas of centrilobular necrosis associated with severe congestion and hepatic hemorrhaging; the hepatocytes showed a high degree of hydropic-vacuolar degeneration.

The kidneys of all birds (5/5) showed hydropic-vacuolar degeneration and acute tubular necrosis, which were associated with pyknosis, karyorrhexis, and karyolysis of the nuclei of tubular cells, cytoplasmic microvacuolation, vascular dilation, and erythroid repletion.

Histology of the skeletal muscle tissue showed intense infiltrate composed of heterophils, lymphocytes, and eosinophils in the skeletal muscle fibers in a multifocal arrangement. The sarcomeres located near the inflammatory infiltrate were swollen and degenerated (Fig. 1E).

The brains of four birds (4/5) showed severe congestion and vasogenic edema, malacia, severe gliosis, and satellitosis. There was also edema and neuropil vacuolation associated with severe vascular congestion.

3. Discussion

The morphometric identification of the type of bee responsible for the attack on the birds was hampered by the absence of samples for identification, but the ferocity of the attacks and the predominance of Africanized honeybees in Brazil strongly suggest that this strain was responsible.

Africanized honeybees attack in swarms, are ready to sting much faster and with much less provocation, and are more persistent in their attacks than their European counterparts (Tunget and Clark, 1993). This behavior is evidenced in the attack on the macaws, since the swarm invaded the bird enclosure without any sign that they had been provoked by the birds; this aggression has earned Africanized honeybees the nickname “killer bees” in some countries (Kim and Oguro, 1999). Like humans (de Oliveira et al., 2000) and domestic animals (Oliveira et al., 2007), wild animals may also suffer massive attacks by Africanized honeybees, although no reports involving parrots were known before the present case.

A. ararauna have blue dorsal feathers and yellow ventral feathers as well as rows of black feathers in their facial and neck regions (Forshaw, 2010; Jupter and Parr, 1998), and *A. chloropterus* (Sick, 2001) have red feathers, green wings, and white faces with narrow red lines (Jupter and Parr, 1998). Although both species were in the same enclosure, the *A. ararauna* birds suffered a greater number of stings that were concentrated in the facial region without feathers. According to Vetter et al. (1999), Africanized honeybees tend to attack the head and neck because, according to Fitzgerald and Flood (2006), these regions are more exposed as the bodies of most animals are covered with feathers or fur. It is known that bee attacks can be triggered by provocation, strong odors, and (in particular) dark colors, and moreover, when bees sting, they release chemicals from their glands at the time and location of the sting, which recruits and directs other bees in the swarm to the same victim (Sherman, 1995).

The clinical signs presented in humans and animals attacked by Africanized honeybees can vary from an allergic reaction to systemic toxicity depending on the number of stings received and the sensitivity and weight of the victim (Cardoso et al., 2003). Deaths from multiple stings can result via three main mechanisms: direct

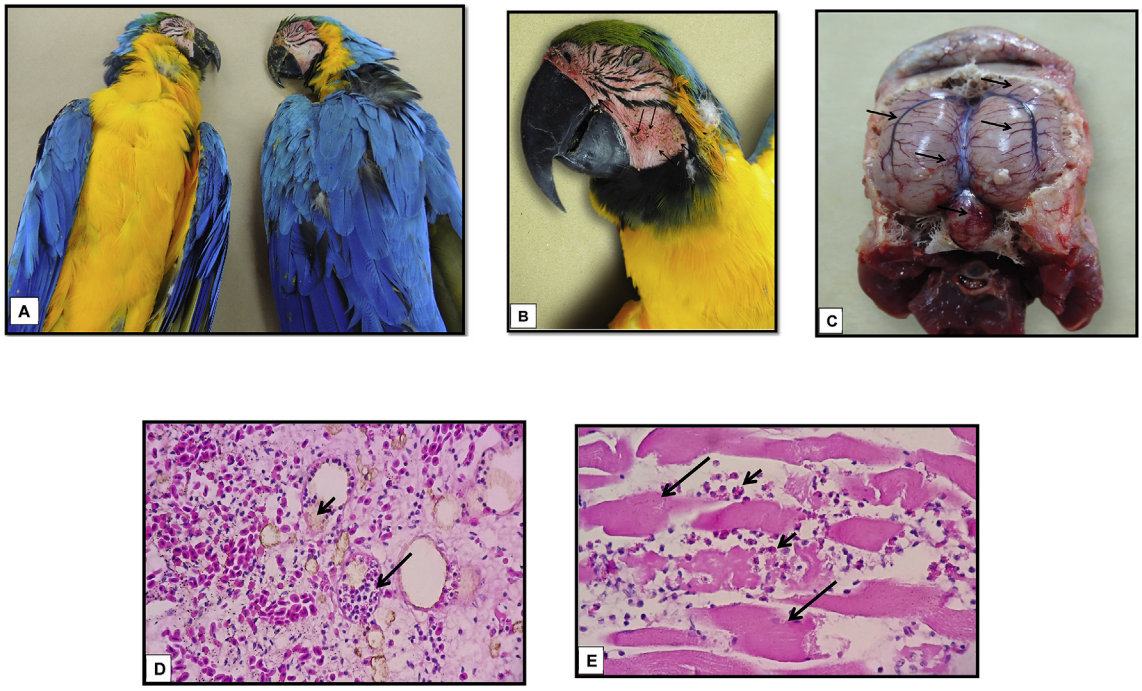

Fig. 1. A). *Ara ararauna* specimens. Note the blisters on the non-feathered facial regions and the regurgitated food adhering to the beak. B). Face of an *Ara ararauna* specimen. Note the large number of stingers in the face (arrows) and facial blisters. C). Brain and cerebellum of *Ara ararauna*. Note the severe congestion of the blood vessels (arrows). D). Photomicrograph of the lung of *Ara ararauna*. Note the intra-alveolar hemorrhage, aspirated food (short arrow), and infiltrate of heterophils (long arrow). HE. Lens: 40× magnification. E). Photomicrograph of the skeletal muscle of *Ara ararauna*. Note the eosinophilic inflammatory infiltrate (short arrow) and the swelling of the muscle fibers (long arrow). HE. Lens: 40× magnification.

toxicity of the venom, intravascular hemolysis caused by melittin, or profound hypotension resulting from the inoculation and release of endogenous histamine. Together, these mechanisms have a cumulative, cascading effect that can result in multiple organ failure represented by acute tubular necrosis and kidney failure, respiratory failure, rhabdomyolysis, myoglobinemia, damage to myocardial cells, hepatocellular necrosis, disseminated intravascular coagulation, and bleeding (Medeiros, 2003).

The affected birds were in adulthood with body weights between 1.3 kg (*A. ararauna*) and 1.5 kg (*A. chloropterus*), and the *A. ararauna* specimens had a greater number of stingers (approximately 63/bird) than the *A. chloropterus* specimens (approximately 45/bird). In humans, the estimated lethal dose is approximately 500 stings per individual or 19 stings/kg body weight (Schumacher et al., 1992; Vetter et al., 1999). The lethal dose for birds, especially those of the Psittacidae family, has not yet been determined but seems to exceed the estimated dose for humans since the birds that survived had received an average of 30 stings/kg of body weight. The clinical signs presented by *A. chloropterus* birds, which showed localized swelling at the sites of the stings and respiratory difficulty, may be characteristic of an acute toxic reaction to the large quantity of injected venom. According to Walker et al. (2005), dogs that exhibited systemic toxic reactions to bee attacks presented vomiting, diarrhea, and respiratory difficulty associated with acute respiratory distress syndrome.

Rahman et al. (2015) reported a massive bee (*Apis mellifera)* attack on 16 pigeons (*Columba livia*), of which nine were adults and seven were squabs. Twenty hours after the incident, only six adult birds survived, and they were subsequently treated with prednisolone sodium succinate (10 mg/kg, IM), diphenhydramine hydrochloride (5 mg/kg, IM), and sulfadimidine sodium (0.2 mg/kg, IM). The clinical signs presented by the pigeons that survived were similar to those presented by the macaws, namely, palpebral edema, congestion of the conjunctiva, generalized edema, edema and erythema around the stingers, and cervical rigidity (Rahman et al., 2015). According to these authors, five of the six surviving pigeons died 12 hours after the start of treatment, and the number of stingers found in each was 4, 5, 9, 10, and 11.

Honeybee venom is composed of enzymes, large peptides, and proteins including melittin, PA2, apamin, peptide 401, hyaluronidase, histamine, dopamine, adrenalin norepinephrine, serotonin, and norepinephrine (Han et al., 2000). The swelling and congestion found in organs during necropsy may result from the toxic effects of the different venom components, including both the vasoactive action of histamine and leukotrienes (Habermann, 1972) and the tissue damage caused by melittin and PA2 (Prado et al., 2010).

In this study, the lungs of all birds (5/5) showed pulmonary edema, diffuse congestion, and hemorrhaging; the congestion and pulmonary edema may be associated with the large amount of histamine injected with the venom or may be the result of endogenous stimulus by other venom components(Schmidt, 1995). These findings, which are characteristic of acute respiratory distress syndrome, are also common in cases where dogs (Oliveira et al., 2007) and humans (França et al., 1994) have suffered massive attack by honeybees (Walker et al., 2005). Here, three birds (3/5) presented contents in the lung parenchyma, which may indicate that the birds suffered seizures during the agonal period that may have been due to the action of the venom components, particularly apamin, a neurotoxic polypeptide that can produce erratic involuntary movements culminating in seizures in high doses (Habermann, 1972).

The cardiac muscle tissue was also affected by the venom, showing necrosis, diffuse congestion, and myocardial infarction. According to (Mjoy, 1988), the melittin, PA2, and histamine in the venom stimulate endogenous secretion of adrenaline and norepinephrine, which may cause myocardial ischemia. Studies conducted in rats have demonstrated the direct toxic action of honeybee venom on the heart muscle, which can cause acute myocardial

infarction (Ferreira et al., 1995, 1994). It is believed that PA2 is responsible for activating arachidonic acid metabolism, during which leukotrienes and prostaglandins are released, and these mediators may be responsible for endothelial relaxation, coronary artery spasms, or myocardial infarction. Moreover, the venom sac contains approximately 2 μg of histamine (Schumacher and Egen, 1995); considering the average number of stings and the weight of the birds, each is estimated to have received, on average, 96 μg/kg of histamine. In humans, it is known that 1 μg/kg of histamine can produce serious cardiac disorders (Schumacher and Egen, 1995).

As in the heart, severe myositis in the skeletal muscles can result from the action of melittin and PA2, which, alone or in synergy, damage biological membranes by hydrolyzing phospholipids, thus inducing pore formation and tissue lysis. Moreover, this may cause hypercontraction and clumping of myofibrils followed by rupture, lysis, and possible infiltration of phagocytic cells (Ownby et al., 1997). Azevedo-Marques et al. (1992) reported that Africanized honeybee venom induced myonecrosis *in vivo* in rats.

Damage to the hepatocytes is one of the consequences of massive wasp and hornet attacks (Weizman et al., 1985), and three birds in this study showed centrilobular necrosis associated with severe congestion and hepatic hemorrhaging. Similar findings are common in bee accidents involving humans (França et al., 1994), but no change has been observed in the livers of dogs that have suffered massive bee attacks (Oliveira et al., 2007).

Acute tubular necrosis is a commonly reported result of poisoning by massive honeybee attacks (Grisotto et al., 2006). The kidneys of four of the five (4/5) macaws displayed hydropic-vacuolar degeneration and acute tubular necrosis, which may be associated with several venom components. Melittin can compromise renal blood flow in different ways: by damaging the vascular endothelium (Schumacher and Egen, 1995), by causing vasoconstriction (Koyama et al., 2002), by stimulating smooth muscle contraction (França et al., 1994), by increasing the secretion of renin (Churchill et al., 1990) and catecholamines (França et al., 1994), and by releasing arachidonic acid (Levine and Hassid, 1977). Additionally, PA2 is related to renal vasoconstriction (Imig and Deichmann, 1997) and can reduce renal blood flow by stimulating the endogenous release of catecholamines and vasoconstrictors (Grisotto et al., 2006). Histamine may also reduce the rate of renal blood flow, causing severe hypotension and acute kidney injury (Grisotto et al., 2006). Catecholamines, such as norepinephrine and dopamine, whether endogenous or from venom, can also alter renal hemodynamics and cause hypertension ((Bourgain et al., 1998; Bresolin et al., 2002; França et al., 1994; Munoz-Arizpe et al., 1992; Sert et al., 1993). Therefore, kidney damage may be secondary; that is, it may be caused by the presence of large amounts of myoglobin released by the rhabdomyolysis triggered by melittin (Ownby et al., 1997; Zager, 1996).

The changes observed in the central nervous system of the necropsied birds differed from those recorded in dogs, which show only vascular congestion. However, an experimental study reported neurotoxic action from bee venom in mice (Habermann and Fischer, 1979; Oliveira et al., 2007).

4. Conclusion

The clinical signs and pathological findings observed in the birds that suffered a massive attack from honeybees are similar to those found in mammals and pigeons.

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