

Key-Gaskell syndrome in Brazil: first case report

[*Síndrome de Key-Gaskell: primeiro relato de caso no Brasil*]

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ABSTRACT

Feline dysautonomia is a devastating disease characterized by neuronal degeneration in autonomic ganglia that results in clinical signs related to dysfunction of the sympathetic and parasympathetic nervous systems. The cause is unknown and this disease has a poor prognosis and no definitive treatment. Most reports have been described in few countries around the world, but the prevalence may be underestimated in countries like Brazil. This study describes the progression and clinicopathological changes of dysautonomia in a 17-month-old female Brazilian shorthair cat.

Keywords: neurology, ganglioneuropathy, feline dysautonomia

RESUMO

Disautonomia felina é uma doença devastadora, caracterizada por degeneração neuronal em gânglios autonômicos, a qual resulta em sinais clínicos relacionados à disfunção dos sistemas simpático e parassimpático. Sua causa é desconhecida, o prognóstico desfavorável e não há tratamento definitivo disponível. A maioria dos relatos foi descrita em países ao redor do mundo, mas sua prevalência pode estar subestimada em países como o Brasil. Este estudo descreve a progressão e as alterações clínico-patológicas da disautonomia em um gato de pelo curto brasileiro, do sexo feminino, de 17 meses de idade.

Palavras-chave: neurologia, ganglioneuropatia, disautonomia felina

INTRODUCTION

Feline dysautonomia, or Key-Gaskell syndrome, is a dysfunction in autonomic nervous systems, due to neuronal degeneration in the nervous ganglia (Sharp *et al.*, 1984). It was first recognized in Scotland (Key and Gaskell, 1982), and since then few cases have been reported (Kidder *et al.*, 2008).

The etiology is unclear although genetic susceptibility and neurotoxin or infectious agents have been postulated (Nunn *et al.*, 2004). There is no sex or breed predisposition but the young animals seem to be most affected (Symonds *et al.*, 1995).

Clinical signs include depression, anorexia and may reflect generalized autonomic dysfunction (Cave *et al.*, 2003; Kidder *et al.*, 2008).

To confirm diagnosis, histopathological examination of autonomic ganglia is required. A marked reduction in neuronal numbers in the ganglia is observed in all cases, regardless of species (Kidder *et al.*, 2008). This disease has a poor prognosis and no definitive treatment is available (O'Brien and Johnson, 2002).

To the best of our knowledge, this disease has never been described in Brazil, perhaps because it is a rare disease or possibly due to underestimated prevalence owing to misdiagnosis. Therefore, the aim of the present report is to describe the clinicopathological features of a cat with generalized autonomic nervous system disorder that was diagnosed with feline dysautonomia.

CASUISTRY

A 17-month-old female Brazilian shorthair cat was admitted to the Federal University of Minas Gerais Veterinary School two days after showing acute clinical signs of prostration, anorexia, difficulty swallowing and regurgitation/vomiting. The animal lived in an urban area confined to a private house with no other in-contact animals. However, the owner reported that the animal had hunted a dove a week before. Standard vaccination and deworming were up to date.

Upon physical examination the cat was depressed, in poor body condition, dehydrated, dyspneic, dysphonic, had dilated unresponsive pupils with discreet anisocoria and a slight rotation of the right eye pupil, reduced tear production, dry and crusty nose (Figure 1a). Besides that, profuse salivation, hypothermia, and abdominal distension due to fecal and urinary retention were observed. Within few hours after being admitted the cat became severely depressed, showing prolapsed third eyelids and its respiratory distress worsened. No important abnormalities were recorded on blood tests. Laterolateral projection of the abdominal radiography showed marked distention of the stomach and small intestine with gas. Bladder distention with urine retention was also observed. Contrasted radiography detected moderate dilatation in all esophageal extension (Figure 1b). Laryngo-tracheo-bronchoscopy showed no obstructive abnormality, however, there was an accumulation of mucus secretion in the respiratory tract. Interestingly, during the anesthetic period miosis was observed in both eyes.

The animal died 72 hours after being admitted. Necropsy was performed and multiple tissue specimens were collected for histological examination. Post-mortem examination showed esophageal dilatation and the lungs were intensely dark red and firm, suggesting aspiration bronchopneumonia. Fragments of the esophagus, small and large intestines and ganglia were collected at necropsy. Histologically, the submucosal and myoenteric plexi from esophagus, duodenum, jejunum, ileum, cecum and colon revealed pronounced loss of neuronal cell bodies and shrinkage neurons. The dorsal roof ganglia presented several degenerate neurons with markedly chromatolytic, peripheral

rosettes of nonstaining cytoplasmic vacuoles and neurons with shrunken, angular bodies with hypereosinophilic cytoplasm and dark pyknotic nuclei (Figure 2). An intense esophageal muscular atrophy was also observed.

DISCUSSION

Feline dysautonomia is a severe disease caused by the degeneration of both the sympathetic and parasympathetic autonomic nervous system (O'Brien and Johnson, 2002). In the present report, after physical examination, image findings and histological features confirmed the diagnosis of dysautonomia in a 17-month-old female Brazilian shorthair cat. This is a rare and devastating pathological condition in domestic cats with very low survival rates. Up to 70% of the affected cats will die or be euthanized at the request of their owners (Sharp *et al.*, 1984; Kidder *et al.*, 2008).

After the first report made by Key and Gaskell (1982), some cases were described in the 1980s and 1990s, mostly in Europe and less frequently in the USA, but since then the incidence has decreased considerably (Kidder *et al.*, 2008). In a retrospective study of 286 cases of neurological disorders affecting cats from 1975 to 1998 in UK, 27 (9%) were diagnosed with dysautonomia. The majority of cases (85%) were diagnosed between 1982 and 1986, with only four cases diagnosed subsequently (Bradshaw *et al.*, 2004).

Substantial evidences have been demonstrated in regard to environment, time spent outdoors, exposure to various types of land, diet, source of drink water and exposure to other animals, however, studies failed to confirm significant correlations (Cave *et al.*, 2003; Kidder *et al.*, 2008). On the other hand, Symonds *et al.* (1995) and Nunn *et al.* (2004) described episodes characterized by the appearance of several cases in the same feline colony, which suggests an infectious or toxic-metabolic cause. The close familial relationship between the most severely affected cats could be suggestive of genetic susceptibility (Cave *et al.*, 2003). Strong circumstantial evidence of an association between feline dysautonomia and *Clostridium botulinum* type C has been provided. Its toxin was detected in samples from the affected cats (Nunn *et al.*, 2004).

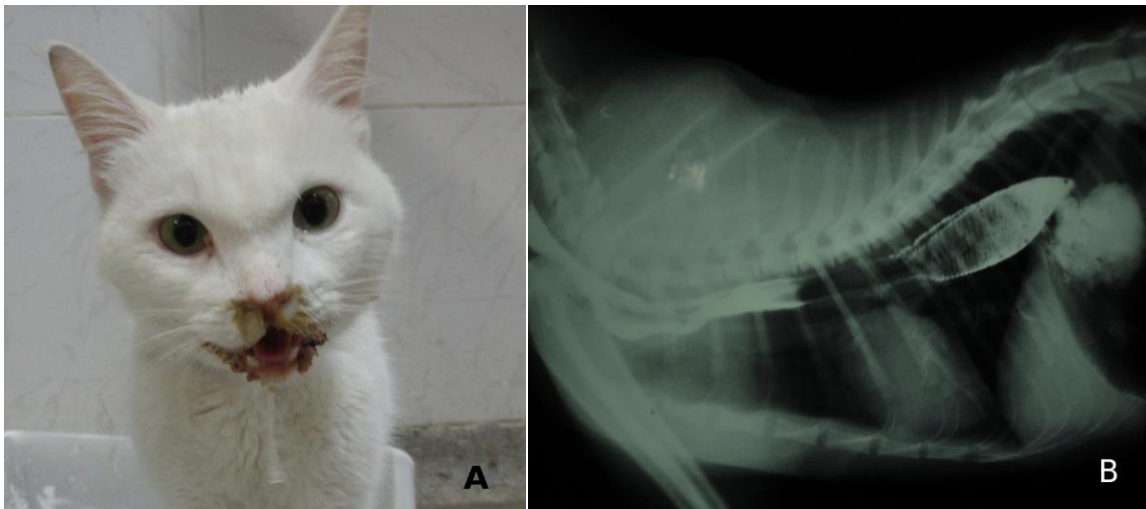


Figure 1. A 17-month-old female Brazilian shorthair cat with feline dysautonomia. **A)** Note dilated pupils, dry and crusty nose and profuse salivation. **B)** Contrasted esophagography with barium sulfate. Note moderate dilation in the entire esophageal extension.

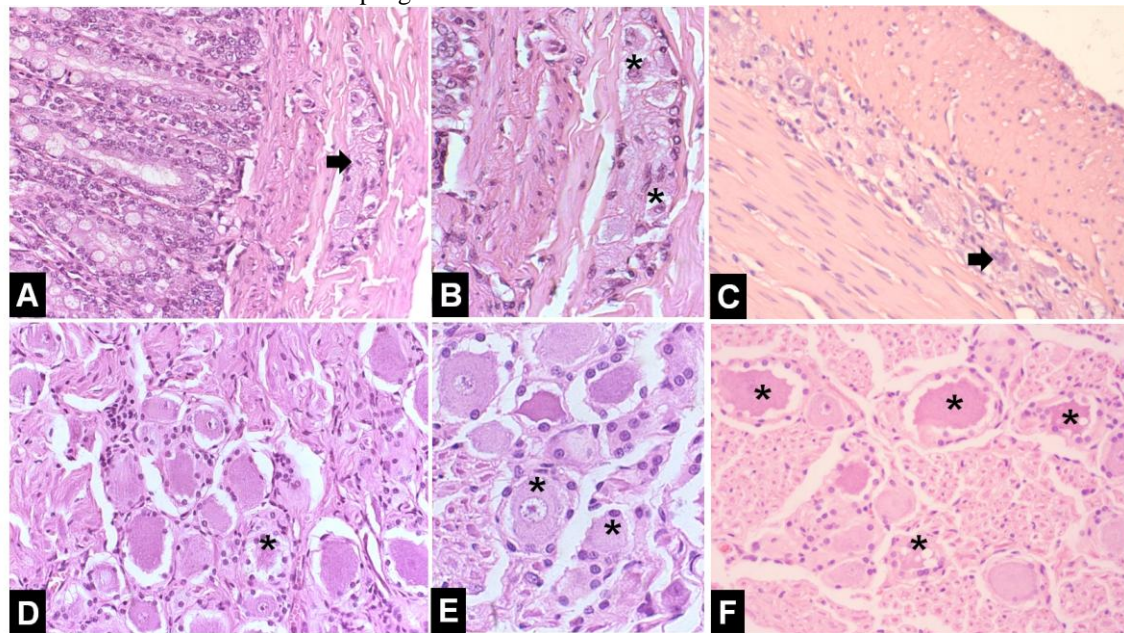


Figure 2. H&E-stained photomicroscopies of a 17-month-old female Brazilian shorthair cat with feline dysautonomia. Group of neurons (arrows) in the submucosa (A) and myoenteric plexi (C) in the colon. Note shrinkage of neurons (asterisks) (B). Dorsal roof ganglion exhibiting abnormal neurons with intense eosinophilia and containing peripheral rosettes of nonstaining cytoplasmic vacuoles (asterisks) (D, F). Neurons with loss of Nissl substance (chromatolysis) (E). Original magnification: A, C: $\times 200$; B, D-F: $\times 400$; E: $\times 600$.

Interestingly, in this report, although the cat used to live in an urban area, he had no outdoor access, nor contact with other animals, however, there was an episode when it hunted and ate parts of a dove. There is no intention in this case to investigate whether there was a toxinfection leading to this disease, but we believe it was an

important feature that should be deeply investigated in further studies.

Lethargy, anorexia, vomiting, dysuria, and labored breathing were nonspecific clinical signs. In cats, dilated pupils, prolapsed third eyelid, regurgitation and constipation are the most

common clinical signs. These signs were observed in more than 75% among 86 documented cases (Sharp *et al.*, 1984) and corroborate the findings in this report. Almost 50% of cats with dysautonomia are bradycardic and may develop very dry mucous membranes (Pollin and Griffiths, 1992). The described patient had no bradycardia and although it was presented with dry nose and ocular mucosa, it was drooling thick saliva, probably as a result of its inability to swallow.

Although diagnostic imaging features are not specific for this disease, if findings in multiple systems are detected along with consistent clinical signs, dysautonomia should be substantially considered (Novellas *et al.*, 2010). Esophageal and gastric distension and signs of paralytic ileus are common radiographic findings. Associated aspiration pneumonia and megacolon appear less commonly. Barium swallow reveals megaesophagus in more than 90% of cases (Pollin and Griffiths, 1992).

Megaesophagus and bronchopneumonia were confirmed at necropsy which may have worsened the clinical state. Moreover, the gut stasis frequently results in an inability to defecate and less commonly there may be problems related to bladder atony, as seen in this report. The absence of obstruction signaled by the contrasted radiographs and the widespread terminal intestinal segments dilation were consistent with functional paralysis. Additionally, the absence of obstruction associated with intense accumulation of mucus secretion in the respiratory tract, observed during the laryngo-trachea-bronchoscopy, suggested inadequate autonomic neural activity.

Subsequent pharmacological testing can be used to confirm loss of autonomic function. Pharmacologic agents used for cats include the administration of dilute pilocarpine ophthalmic solution, subcutaneous injection of atropine, and intradermal administration of histamine (Kidder *et al.*, 2008). Miosis after instillation of dilute pilocarpine is consistent with dysautonomia and reflects denervation-induced hypersensitivity of the iris ciliary muscle for parasympathetic agonists. It is worth mentioning that most anesthetic or sedative agents, with the exception of ketamine, will cause miosis (Collins *et al.*,

1995). Therefore, the fact that the animal had mydriasis unresponsive to light stimulation, associated with the development of miosis just after the application of the anesthetics, further strengthens the clinical suspicion of dysautonomia.

Clinical signs develop within 48 hours in most cases, and if the prognosis is unfavorable, there is a mortality rate of approximately 70% (Sharp *et al.*, 1984). In the present case, the progression of clinical signs occurred acutely and due to clinical deterioration despite supportive treatment, five days after the beginning of treatment the animal died.

Definitive diagnosis of feline dysautonomia is based upon demonstration of histological lesions in the autonomic ganglia (Kidder *et al.*, 2008). Chromatolytic neurons within the autonomic ganglia are considered confirmatory of the clinical diagnosis. It is known that the depletion of ganglion neurons and its degenerative features should be observed in cases of dysautonomia, regardless of the species (O'Brien and Johnson, 2002; Kidder *et al.*, 2008). The central nervous system is rarely affected. Bradshaw *et al.* (2004) examined brain tissue from 10 of the 27 cases studied, one of which showed mild vacuolation of the white matter in the obex region, but no other lesions affecting brain or spinal cord of the remaining cats with typical ganglionic lesions were identified. This absence of lesions affecting brain or spinal cord was also reflected in the present study that showed a pathological pattern similar to those extensively reviewed elsewhere (O'Brien and Johnson, 2002; Kidder *et al.*, 2008).

There is no reason as to why the incidence of the disease decreased after 1990s, and even though the cause continues unclear. It is possible that there is an ongoing presence of the disease in the worldwide cat population. The observation of altered esophageal motility in apparently unaffected cats may suggest a subclinical form of the disease (Cave *et al.*, 2003). This illustrates the difficulties involved in attempting to gather information on disease occurrence. It is believed that this is the first described case of feline dysautonomia in Brazil, since it was not possible to find any reports of this disease in the current literature in several searched databases.

CONCLUSION

Feline dysautonomia, although considered to be rare, is a devastating disease with a poor prognosis and should be investigated in any cat that presents a set of autonomic nervous systems dysfunctions. Most reports have been described in few countries around the world, but there may be a higher incidence of dysautonomia in other countries like Brazil, where the prevalence may be underestimated.

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