CASE REPORT

Cerebellar cortical abiotrophy in a Samoyed dog

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Received: 06.10.2012, Accepted: 02.11.2012
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Özet

Saberi M, Kheirandish R, Azizi S, Mohebbi E. Bir Samoyed köpekte serebellar kortikal abiotrofi. **Eurasian J Vet Sci, 2014, 30, 1, 44-47**

Serebellar abiotrofi birçok hayvan türünde cinsiyetten bağımsız, otozomal, kalıtsal nitelikte tipik olarak Purkinje hücrelerinin progresif kaybıyla karakterize bir durumdur. Mevcut vakada travma veya başka hastalık hikayesi olmayan ataksi gözlenen bir haftalık Samoyed ırkı bulunmaktadır. Fiziksel muayenede kontrolsüz hareketler, gövdede ılımlı ataksi ve başta şiddetli titremeler gözlendi. Ayrıca köpek yerken sıkıntılı, otururken ve yürürken düşmeden sıkıntılı gözlendi. Hastada tam kan, serebrospinal sıvı analizi ve serebral radiyografi normal gözlendi. Tedavide uygulanan diazepam, vitamin B_1 ile glukokortikoidler klinik belirtiler üzerine etkili olmadı ve bir ay sonra köpek öldü. Klinik ve histopatolojik belirtilere göre serebellar kortikal abiotrofi olgusu tanımlandı. Mevcut vaka Samoyed ırkı köpekte tanımlanan ilk serebellar kortikal abiotrofi özelliğinin taşımaktadır.

Anahtar kelimeler: Samoyed, serebellar abiotrofi, granular hücreler, Purkinje hücreleri.

Abstract

Saberi M, Kheirandish R, Azizi S, Mohebbi E. Cerebellar cortical abiotrophy in a Samoyed dog. **Eurasian J Vet Sci, 2014, 30, 1, 44-47**

Cerebellar abiotrophies have a non-sex-linked, autosomal, recessively inherited basis in anumber of animal species, and lesions typically reflect progressive loss of Purkinje cells. In this report, ataxia was observed in a one-week-old male Samoyed puppy with no history of trauma or any other illness. Physical examination revealed uncoordinated movements, mild trunkal ataxia and intensive head tremors, so the dog had trouble eating, evacuating and difficulties in standing and walking without falling. The complete cell count, cerebrospinal fluid analysis and cerebral radiographs were normal. Treatment with diazepam, vitamin B_1 and glucocorticoids had no effect on clinical signs and the dog died after a month. According to clinical signs and histopathological features, cerebellar cortical abiotrophy was diagnosed. This is the first report of a cerebellar cortical abiotrophy in a Samoyed puppy

Keywords: Samoyed, cerebellar abiotrophy, granular cells, Purkinje cells.

Cerebellar cortical abiotrophy is a postnatal syndrome and havea non-sex-linked, autosomal, recessively inherited basis in a number of animal species suchas Airedales (Cordy and Snelbaker 1952), Labrador retriever (Bildfell et al 1995), miniature schnauzer (Berry and Blase-Machado 2003), and Swedish Lapland dogs (Sandefeldt et al 1973). The affected animals are normal at the birth time but after a few weeks, the disease slowly progresses with cerebellar ataxia. The clinical signs may not appear for a year or more, in a few breeds. The major lesion is an intrinsic degeneration of the Purkinje neurons causing by genetic abnormality in the cell's metabolic system. Severity of the lesions depends on how long degenerative changes are progressed (Sandy et al 2002, Mouser et al 2009).

This study describes the occurrence of cerebellar cortical abiotrophy in a Samoyed dog. A one-week-old male, Samoyed puppy referred to Veterinary Teaching Hospital of Shahid Bahonar University of Kerman, Iran, with pelvic limb stiffness and ataxia in four appendages limbs and head tremor. The puppy showed evidence of a gait abnormality which had progressed to a mild base wide ataxia involving all four limbs. Although the gait was dysmetric but there was no obvious loss of position sense of the limbs. Postural reactions were intact but the response delayed and spastic. Proprioceptive positioning usually is normal. A head tremor which occurred as side-to-side and to-and-fro motions became exaggerated with intended head movements. The dog also had a mild trunkal ataxia. No abnormal nystagmus was observed. The menace response (ipsilaterally) was absent although normal facial nerve function and vision were normal. The dog was not completely alert and slept more than normal puppies. The animal was kept under observation for four weeks prior to death. During this period, a pronounced trunkal ataxia with side-to-side and to-and-fro oscillations of the body developed. All movements involving the head, limbs and trunk were disorganized and jerky, falling backwards occurred frequently. All observed clinical signs were in consistent with cerebellar dysfunction. The referring veterinarian performed a complete blood cell count, serum biochemical profile, and fasting and postprandial bile acids analysis at age 1w; the results were normal. The treatment course was started with diazepam (1 mg/kg), vitamin B_1 (1-2 mg/kg/day), and prednisolone acetate 1% (2.5-5 mg/kg/day). The dog had no response to the treatment and died after a month. Due to owner request and after taking consent, the necropsy was performed immediately. No remarkable gross abnormalities in any organs at postmortem examination were found. Tissue samples of the cerebrum, cerebellum and spinal cord were fixed promptly in 10% neutral-buffered formalin, dehydrated in graded ethanol, cleared with xylene, and embedded in paraffin. Sections in 5µm thickness were routinely stained with haematoxylin-eosin (HE). Degeneration was evident in microscopic examination of the cerebellum; however, there was not macroscopic lesion on the brain. Histopathologically, the molecular layer of cerebellar cortex was depleted and thin due to loss of neuronal processes. Purkinje cells were depleted obviously. Remained Purkinje cells in affected folia displayed swelling of the perikaryon, karyolysis, and dispersion of Nissl substance around (central chromatolysis). The granular layer was hypocellular, with scattered pyknotic nucleoli that suggests apoptotic remnants. A few ectopic Purkinje cells were observed in this layer. White matter was narrow and its depth in cerebellar folia was reduced (Figure 1). Wallerian degeneration was occurred in the white matter and axonal spheroids in low numbers were visible (Figure 2). Based on the clinical signs and microscopic lesions, a diagnosis of cerebellar abiotrophy was made.

Cerebellar cortical abiotrophy (CCA) is degeneration in central nervous system that results from spontaneous, premature and progressive neuronal degeneration and death (Summers et al 1995). This degeneration occurs because of intrinsic metabolic defect which leads to programmed cell death as a part of normal developmental processes in affected tissues. Most of the abiotrophies are considered to be inherited but the genetic basis of many of them is not yet established. Some of the reports, including our case, have not been proven to be genetic. The inheritance of the CCA is reported to be an autosomal recessive gene (de Lahunta 1990), expressed when inherited as a homozygous condition.

CCA represents a collection of postnatal syndromes that are progressive and incurable. It occurs in a wide range of species such as Kerry Blue Terrier, Gordon Setter, Rough-Coated Collie, Australian Kelpie, Airedale, Brittany Spaniel, Border Collie, Beagle, Irish Setter, Labrador Retriever, and Rhodesian Ridgeback (Cordy and Snelbaker 1952, Palmer et al 1973, de Lahunta and Averill 1976, Hartley et al 1978, de Lahunta et al 1980, Gill and Hewland 1980, Yasuba et al 1988, Thomas and Robertson 1989, Tatalick et al 1993, Chieffo et al 1994, Bildfell et al 1995). In this study, we described the clinical signs and pathologic findings of cerebellar abiotrophy which were in agreement with those reported by de Lahunta (1990). To our knowledge, this is the first report of CCA in a Samoyed dog.

Age of onset of clinical signs is variable, with 3 general categories identified: 1) early onset between two and three weeks, like the Beagle, Miniature poodle, and Rough-coated Collie, 2) mediate onset between five and16 weeks like the Kerry blue terrier, Border Collie, Australian Kelpie, and Labrador Retriever, and, 3) atypical late onset between six and24 months like the Gordon Setters and Brittany Spaniels (Tatalick et al 1993). The case presented here was one-week-old and its signs were observed at the beginning of the second week. In early-onset group, a fast progression of cerebellar ataxia has been described, similar to that seen in our Samo-

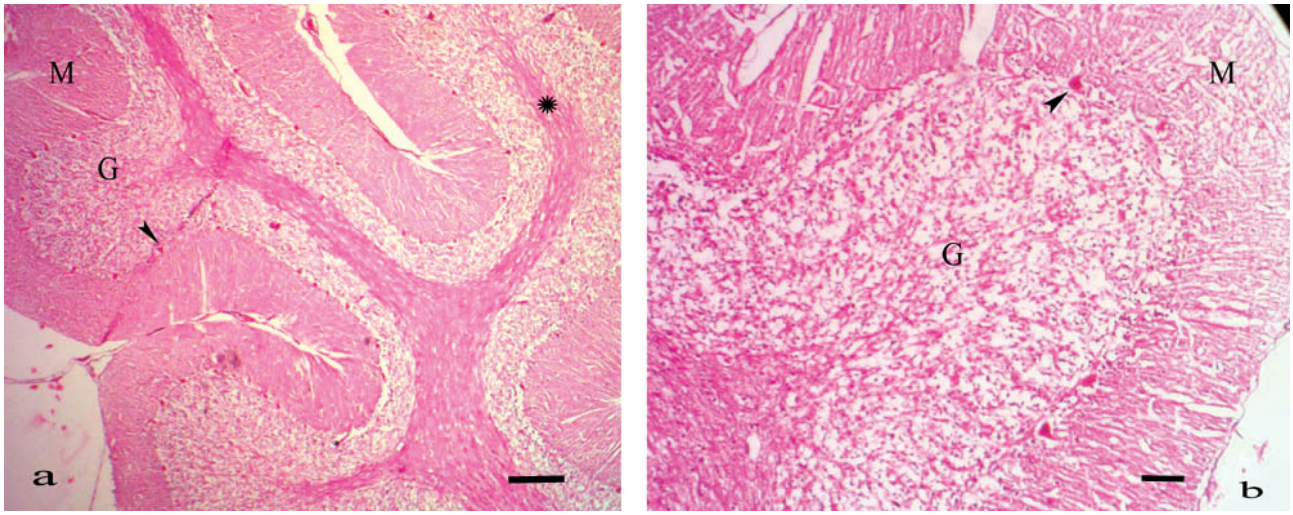

Figure 1. a) Histopathologic findings of cerebellar abiotrophy reveal thin molecular layer (M), severe depletion of granular (G) and Purkinje cells (arrow). The depth of white matter in cerebellar folia was reduced (asterisk) (H&E, Scale bar=250 µm) (b) The lesions are visible in higher magnification (H&E, Scale bar=100 µm).

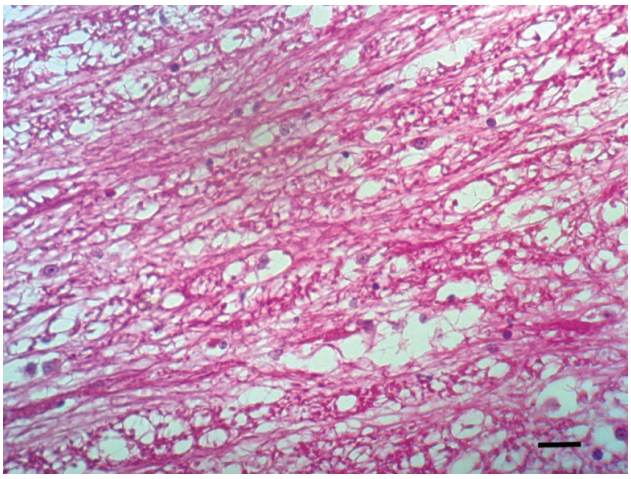

Figure 2. White matter of the cerebellum shows Wallerian degeneration that characterize with vacuolation of myelin (H&E, Scale bar=25µm).

yed puppy, whereas in animals with late-onset disease the signs are often slowly progressive (Thomas and Robertson 1989).

Moreover, the speed of progression varies with the breeds that are affected with this abnormality. In some breeds, progression is almost rapid (Chieffo et al 1994, Tipold et al 2000, van Tongern et al 2000, Berry and Blase-Machado 2003), and results in the inability to coordinate to stand. In others, the gait disorder is very mild and does not incapacitate the animal.

The pathogenetic mechanisms leading to cerebellar abiotrophy is currently obscure, but is presumed to be an intrinsic metabolic defect. One hypothesis represents excessive glutamate could cause degeneration of the neuron. Excessive glutamate stimulation is caused by various ways including excessive glutamate release, decreased glutamate uptake and clearance, or increased glutamate receptor sensitivity. The cerebellar glutamate accumulation abnormalities could be due to inherent defects in the metabolism of glutamate, but could also be caused by damage associated with hypoxia or hypoglycemia (de Lahunta 1990). The excitotoxic degeneration of neurons by glutamate has been proposed in Kerry Blue Terriers (de Lahunta and Averill 1976).

Histopathologic lesions depend on how long the degeneration has been progressed. The degree of degeneration is categorized to acute and chronic cases. In acute cases, an ischemic degeneration in Purkinje neurons could be observed. However, in chronic cases, the depletion of Purkinje neurons and accumulation of astrocytes (Bergman astrocytes) are confirmed. In most animals, the granular layer neurons will also be depleted. In described dog, at necropsy there were any macroscopic signs of cerebellar abnormalities like thrombosis, infarction, hemorrhage or mass. However, the cerebellar cortex had obvious depletion of Purkinje cells. Remained Purkinje cells in affected folia displayed swelling of the perikaryon, karyolysis, and dispersion of Nissl substance around (central chromatolysis). The granular layer was hypocellular, with scattered pyknotic nucleoli that suggests apoptotic remnants. A few ectopic Purkinje cells were observed in this layer. The molecular layer was depleted and thin due to loss of neuronal processes. White matter was narrow and its depth in cerebellar folia was reduced. Wallerian degeneration was occurred in the white matter and axonal spheroids in low numbers were visible. To our knowledge, this is the first reported case of cerebellar abiotrophy in the Samoyed dog.

Although several diagnostic methods were used, only after post mortem examination and histopathology was a definitive diagnosis of cerebellar cortical abiotrophy made. Histopathologic findings of cerebellar abiotrophy reveal thin molecular layer, severe depletion of granular, and Purkinje cells. Despite a few reports in many various dogs breed, this the first report of CCA in Samoyed dog.

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