Cerebellar hypoplasia in an Azawakh dog: A case report

Azawakh ırkı bir köpekte Cerebellar Hypoplasia: Olgu sunumu

ABSTRACT

In this case report, a nine-month-old male Azawakh dog was observed for ataxia, uncoordinated movements, and difficulties in walking and standing, intensive head tremors, trouble evacuating and eating. It was determined to have mild cerebellar hypoplasia in MR imaging and symptomatic treatment was started with glucocorticoids, vitamin B_1, B_6 and diazepam. But these drugs had no effectiveness on the symptoms and the dog died three weeks later. In the necropsy macroscopic cerebellar reduction was determined and cerebellum and granular cell hypoplasia was indicated histopathologically. Immunohistochemically, the atrophy of neuronal cells showing positive staining with anti-GFAP antibody and vacuolar degeneration were identified.

Based on clinical findings, MR imaging, histopathological and immunochemical findings, cerebellar hypoplasia was diagnosed in the dog and this study is the first case detected in an Azawakh dog.

Keywords: Azawakh, dog, cerebellar hypoplasia, granular cells.

ÖZET

Bu olgu sunumunda, dokuz aylık erkek Azawakh ırkı köpek, ataksi, koordinasyon bozukluğu, yürüme ve ayakta durma zorluğu, başta titremeler, dışkılama ve yemek yemede zorluk çekme şikâyeti ile kliniğimize getirildi. Manyetik rezonans (MR) görüntülemede hafif serebellar hipoplazi saptandı ve semptomatik tedavi amacı ile glukokortikoid, vitamin B_1, B_6 ve diazepam kullanıldı. Ancak köpek üç hafta sonra hayatını kaybetti. Nekropsisi yapılan köpekte makroskobik olarak cerebellar küçülme tespit edilirken, histopatolojik olarak serebellum ve granüler hücre hipoplazisi belirgindi. İmmunohistokimyasal olarak ise anti-GFAP antikoru ve vakuolar dejenerasyonu ile pozitif boyanma gösteren nöronal hücrelerin atrofisi belirlendi.

Klinik bulgular, MR görüntüleme, histopatolojik ve İmmunohistokimyasal bulgular doğrultusunda köpekte cerebellar hypoplasia teşhis edilmiş olup Azawakh ırkı köpekte tespit edilen ilk olgu olması nedeni ile önem taşımaktadır.

Anahtar Kelimeler: Azawakh, köpek, serebellar hipoplazisi, granüler hücreler.

INTRODUCTION

Congenital abnormalities in the brain occur sporadically in domestic animals. Congenital cerebellar disorders can be categorized into three groups: utero or neonatal (usually viral) infections, genetic or unknown cause cerebellar malformations and cerebellar abiotrophies (Johnson et al., 1974; Summers et al., 1995; Schatzberg et al., 2003; Noureddıne et al., 2004; Lım et al., 2008).

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Case Report

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The disease can be caused by viral or bacterial infections, poisoning, malnutrition, damage or general accidents during development in the fetus. Cerebellar hypoplasia is seen most often in cats after in utero panleukopenia infection; it is rarely seen with parvovirus infection of the developing cerebellum in dogs; it may be isolated malformation without infection (Troxel, 2012; Thompson, 2014). The clinical signs are present when the patient first starts to ambulate and are not progressive (Troxel, 2012). This is a condition in which there is loss of the Purkinje cell layer and hypoplasia of the granular cell layer in the cerebellum due to disease affecting the cerebellum prior to birth or very soon after birth. The typical microscopic features of cerebellar hypoplasia are decreases of both Purkinje cells and granule cells (Sullıvan, 1985; Tago et al., 1993; Troxel, 2012). These disorders have traditionally been diagnosed by histologic examination at necropsy or with cerebellar biopsy. However, characteristic changes may be seen on MR imaging (Chrisman et al., 2003).

This study for the first time describes the occurrence of hereditary cerebellar hypoplasia in an Azawakh dog.

MATERIAL METHOD

A nine month old male Azawakh dog who had been vaccinated and had no history of illness was referred to Harran University Veterinary Faculty, Animal Hospital, Department of Internal Medicine where physical examination revealed uncoordinated movements, difficulties in walking and standing, intensive head tremors, ataxia and trouble evacuating and eating. Treatment was started after MR. Symptomatic treatment was started with prednisolone acetate 1% (Prednol®, Mustafa Nevzat, Turkey, 2.5-5 mg/kg/day), vitamin B_1, B_6 (Nervit®, Vetaş, Turkey, 10 mg/kg/day) and diazepam (Diazem®, Deva, Turkey, 1 mg/kg). The dog showed no response to the treatment and died 3 weeks later after a poor prognosis. Cerebellar hypoplasia may show similar symptoms with dandy-walker, lissencephaly and abiotrophy. Dandy-Walker Malformation (DWM) is distinguished from cerebellar hypoplasia by the presence of a triple neuropathological triad, including cystic enlargement of the 4th ventricle, hypoplasia of the cerebellar vermis and hydrocephalus (Hart et al., 1972; Jha et al., 2012). In lissencephaly, it exhibits flattening on the surface of the brain and gyrus, and a decreased number of sulcus (Dobyns and Truwit, 1995). In cerebellar abiotrophy, there is an abnormal development of germinal populations of neuroepithelial cells, unlike cerebeller hypoplasia (Lahunta, 1990; Summers et al., 1995).

Magnetic Resonance (MR) Imaging; General anesthesia was maintained with 0.1 mg/kg xylazine hydrochloride I.M., (Rompun®, Bayer, Turkey) and 10 minutes later ketamine hydrochloride 20 mg/kg I.M., (Ketasol®, Richterpharma, Austria). The anesthetized dog was imaged in sternal recumbency, using a human head coil for stabilization. Image sequences included T1-T2 weighted images (Magnetom Symphony, 1.5 Tesla, Siemens, Germany).

Histopathology; Tissue samples of the spinal cord, cerebellum and cerebrum were fixed quickly in 10% neutral-buffered formalin for histopathological evaluation. Afterwards they were dehydrated in graded ethanol, cleared with xylene, and embedded in paraffin. Sections of 5 µm thickness were routinely stained with haematoxylin-eosin (HE).

Immunohistochemistry; the sections were taken into polylysine-coated slides run from the same block for immunohistochemical staining. Biosystems Leica Bond-Max automatic painting system with anti-GFAP and anti-S100 was signed with primary antibodies. The sections to prevent endogenous peroxidase

were held for 5 minutes with 3% H_2O_2 in cross-sections for antigen recovery. Citrate Buffer (pH 0.6) was kept for 20 minutes. A biotin-labeled polyvalent secondary antibody with 30 minutes, streptavidin-peroxidase enzyme for 30 minutes, 3,3'diaminobenzidine (DAB) with the chromogen for 10 minutes, sections incubated for was kept for 3 minutes hematoxylin career for painting then background.

RESULTS

A combination vaccine was done with an Azawakh breed dog which showed neurological symptoms and three of the four male pups born the same day were showing the same nervous symptoms but the owner of the dog did not want to bring the others for examination. Under examination, uncoordinated movements, difficulties in walking and standing, intensive head tremors, ataxia and trouble evacuating and eating were revealed. All movements involving the head, limbs, and trunk were disorganized and jerky and falling backward occurred frequently. Hence, a cerebellar disease was suspected. It was determined to be mild cerebellar hypoplasia in the magnetic resonance imaging (T2 Weighted, sagittal plane) (Figure 1). The patient did not improve during treatment and remained stable. It died three weeks later. There was no notable major abnormality in any organs at the postmortem examination. The patient did not respond to treatment and in the necropsy findings, macroscopic investigations, cerebellum lobules mild hypoplasia, and sulcus was determined with atrophy. Cross-sections of the narrow cerebellar cortex, the medulla, were observed with hyperemia (Figure 2). In a histopathological examination, as identified in the region in the cerebellum granular cell hypoplasia was evident. We found demyelinated areas with vacuolar degeneration in different sizes in medullary of the white material (Figure 3).

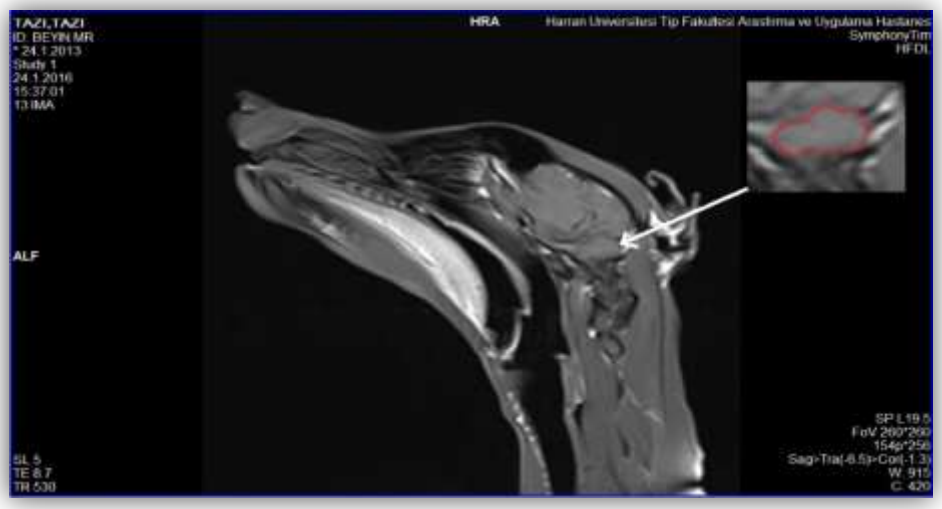

Figure 1. Apperance of mild hypoplasia at cerebellum in T2 Weighted, sagittal plane. Cerebellar hypoplasia appears as a marked reduction in size of the cerebellum (white arrow and window)
Şekil 1. T2 kısmında serebellumda hafif hipoplazi, sagital düzlemde. Serebellar hipoplazi, serebellumun büyüklüğünde belirgin bir azalma (beyaz ok ve pencere)

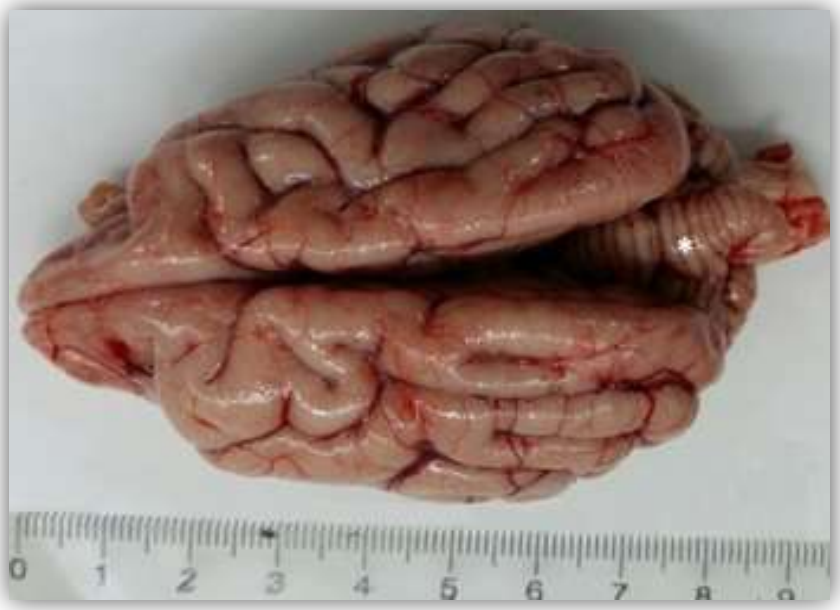

Figure 2. Mild hypoplasia at cerebellum (*), and atrophy at sulcus
Şekil 2. Serebellumda (*) hafif hipoplazi ve sulkusta atrofi

Not understandable. Pyknotic nuclei and cell degeneration in these places were the difference. These regions showed an increase in astrocytic glial cells. We identified central chromatolysis in some neurons. Immunohistochemically, the atrophy of neuronal cells showing positive staining with anti-GFAP antibody and vacuolar degeneration was identified (Figure 4). In particular, it drew the attention to astrocytic cells which reacted positively to demyelinated areas. However, many were observed to be positive to anti-S100 antibodies in the area of spinal gitter cells (Figure 5).

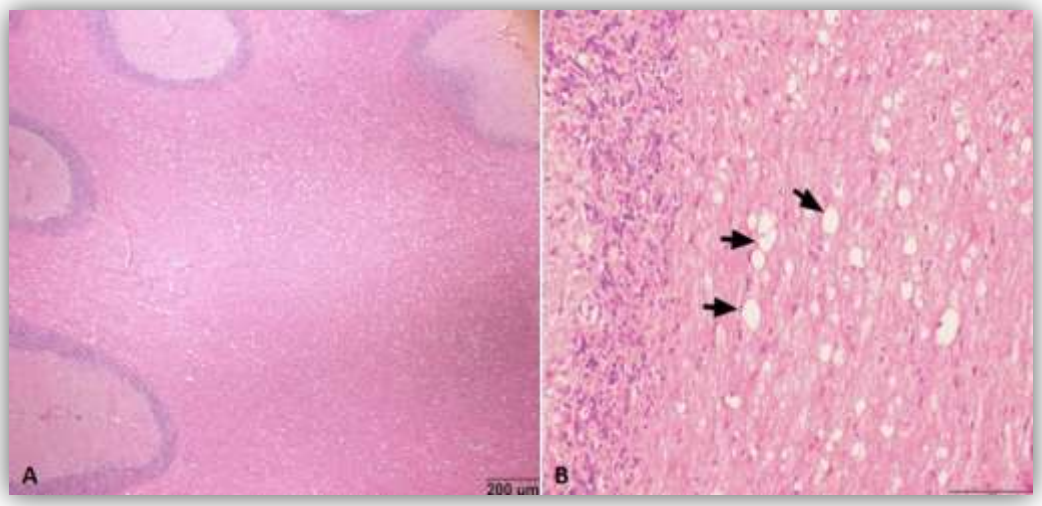

Figure 3. White matter of the cerebellum shows intense vacuolar changes and demyelination (A). Vacuolation of intracytoplasmic (B)
Şekil 3. Serebellumun beyaz maddesi yoğun vakuolar değişiklikler ve demiyelinizasyon (A). İntrasitoplazmik vakuolizasyon (B)

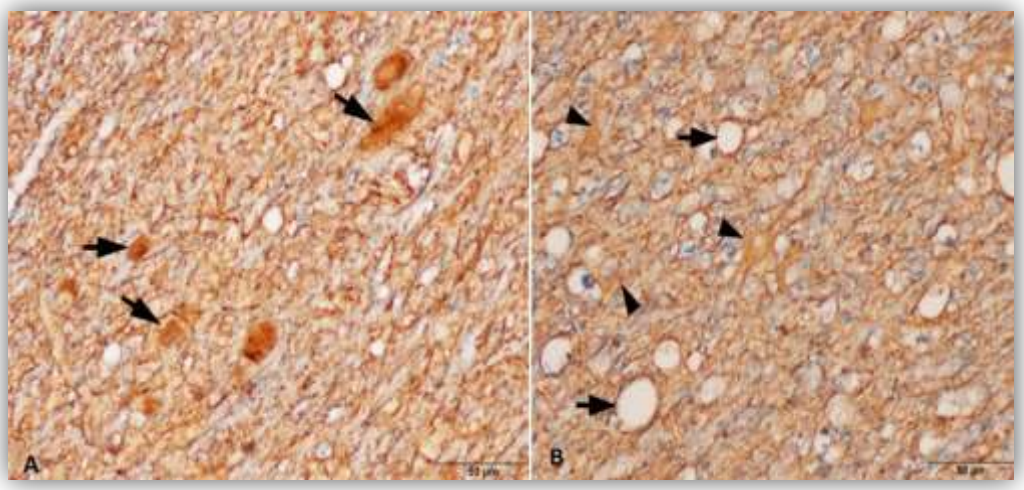

Figure 4. Central chromatolysis in neurons (A). Intense anti-GFAP-positive astrocytic nerve cells (arrowheads), and cytoplasmic vacuolization (B)
Şekil 4. Nöronlarda sentral kromatolizis (A). Yoğun anti-GFAP-pozitif astrositik sinir hücreleri (ok başları) ve sitoplazmik vakuolizasyon (B)

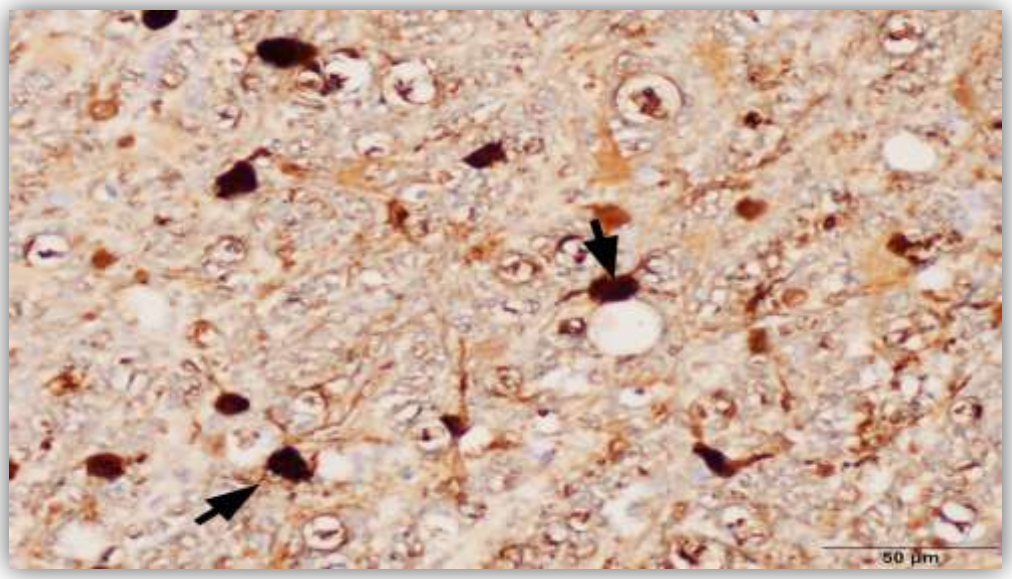

Figure 5. Anti-positive astrocytes S100 cells
Şekil 5. Anti-pozitif astrositler S100 hücreleri

DISCUSSION

Cerebellum development begins in the womb and continues until after delivery, depending on the species. Development continues up to 75 days in dogs, 84 days in cats and 6 months in calves (De Lahunta and Glass, 2009). The cerebellum at cerebellar hypoplasia is smaller than normal. Computerized tomography or MR imaging may demonstrate a small cerebellum and a small cerebellum was also found on necropsy (Chrisman et al., 2003). Clinical findings may vary according to the affected area and grade. Some symptoms appear immediately after birth, while others may appear later. Puppies can fall behind their siblings in sucking, swallowing and movement. As the offspring grow, the symptoms become evident. The puppy can show symptoms such as ataxia, tremors,

turning and bending, head shaking, falling, defecation, and difficulty eating, rather than standing and walking. Some animals may never walk (De Lahunta and Glass, 2009). Cerebellar hypoplasia has been previously diagnosed in relation to uterine viral infection in cats (Csiza et al., 1972), pigs (Emerson and Delez, 1965) and cattle (Brown et al., 1974). In addition, hereditary cerebellar hypoplasia has been diagnosed in cattle (O'Sullivan and McPhee, 1975) and dogs (Cordy and Snelbaker, 1952; Palmer et al., 1973; Knecht et al., 1979). Cerebellar hypoplasia in dogs has been reported in the Chow-Chow, Irish setter, Miniature schnauzer, Bull terrier, Wire fox terrier, and Boston terrier (Chrisman et al., 2003; Choi et al., 2007). In addition, cerebellar vermian hypoplasia has been detected in different breeds (Labrador retriever, Bull terrier, Weimaraner, Dachshund), whose ages ranged from 2 weeks to 32 weeks (Kornegay, 1986). Cordy et al. (Cordy and Snelbaker, 1952) found cerebellar shrinkage and microscopically detected haematoxylin-eosin findings that were detected macroscopically in the airedale breed dog with cerebellar hypoplacia and degeneration which support our case. Kornegay (Kornegay, 1986) showed the presence of chromatolysis and cytoplasmic vacuolization in many neurons microscopically in different dog breeds with cerebellar vermian hypoplasia. The microscopic findings he found were compatible with ours. In the MR examination of our case, hypoplasia in the cerebellum was observed in the T2 part of the case. In a study by Thomson et al. (Thomson et al., 1993), a 6-week-old cat with cerebellar hypoplasia was diagnosed as midline sagittal T1-weighted and MR images coincided with our case.

As a result, we have detected for the first time cerebellar hypoplasia in an Azawakh dog, based on the patient's clinical symptoms, magnetic resonance imaging, necropsy findings, histopathology and immunohistochemistry results. Since cerebellar hypoplasia was detected for the first time in the Azawakh breed dog, it was thought to contribute to the literature.

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The authors declare that there are no conflicts of interest.

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