Arnold-Chiari Malformation in a Captive African Lion Cub

Authors: Shamir, Merav H., Horowitz, Igal H., Yakobson, Boris, and Ofri, Ron

Source: Journal of Wildlife Diseases, 34(3) : 661-666

Published By: Wildlife Disease Association

URL: https://doi.org/10.7589/0090-3558-34.3.661

Journal of Wildlife Diseases, 34(3), 1998, pp. 661–666

Arnold-Chiari Malformation in a Captive African Lion Cub

Merav H. Shamir,[1,4] Igal H. Horowitz,[2] Boris Yakobson,[3] and Ron Ofri,[1] [1] The Koret School of Veterinary Medicine, Hebrew University of Jerusalem, Rehovot 76100, Israel; [2] Tel-Aviv Ramat-Gan Zoological Center (Safari), Ramat Gan, Israel; [3] The Department of Pathology, Kimron Veterinary Institute, Ministry of Agriculture, Beit Dagan, Israel; and [4] Corresponding author (e-mail: shamir@agri.huji.ac.il)

ABSTRACT: Progressive ataxia, delayed growth, dementia and tremors were noted in a female African lion (*Panthera* leo) cub at the Tel-Aviv Ramat-Gan Zoological Center (Israel). The lioness was 3-mo-old when clinical signs were first noticed. Repeated neurological evaluations and blood tests were conducted in an attempt to establish a diagnosis. A congenital abnormality was suspected and the lioness died 6 mo later. Post mortem examination revealed an Arnold-Chiari malformation. The abnormality was classified as a Chiari type 2 malformation, based on the herniation of the cerebellar vermis and paravermis and the slight caudal displacement of the medulla, combined with lack of displacement in other parts of the brainstem.

Key words: African lion, Arnold-Chiari malformation, case history, cerebellum, congenital malformation, medulla, *Panthera leo*.

In March 1996 a female African lion (*Panthera leo*) cub was born at the Tel-Aviv Ramat-Gan Zoological Center (Tel Aviv, Israel; 32°3′N, 34°46′E). Parturition was unremarkable, and the lioness and its male littermate were raised normally by their mother. Both cubs were vaccinated against feline rhinotracheitis, calici and panleukopenia viruses, and were dewormed. Three months after birth the female cub began displaying signs of an abnormal head posture when at rest. The head was slightly elevated and tilted to the right. A fine head tremor, most pronounced when the head was lowered, could be detected. At times the head would actually strike the floor. The lioness was eating and drinking with normal appetite, although she consumed smaller quantities than her male littermate. Progression of the clinical signs was noted over the next 3 mo. The animal's growth rate was slower than normal, and she was noticeably smaller than her littermate. Her coat was dull and dirty. The lioness would spend most of the day lying in the corner and was reluctant to move around the cage. When forced to move about, its gait was unstable and hypermetric. At this time, the lioness' mental status was classified as moderate dementia or depression. When objects were introduced into the cage, she made no attempt to catch or avoid them, even though she could clearly see and follow these objects. This behavior was in marked contrast to that of her littermate, who would instantly attack all new objects. The right head tilt was more pronounced and the lioness was unable to fully control her head movements. The menace response was normal, and no nystagmus or circling were noted. As a result of the deterioration it was decided to anesthetize the lioness for a complete physical and neurological examination. The animal was anesthetized with an intramuscular injection of ketamine (Fort Dodge Laboratories, Inc., Fort Dodge, Iowa, USA) (10 mg/kg) and diazepam (Hoffman-LaRoche Inc., Nutley, New Jersey, USA) (1 mg/kg). The lioness weighed 40 kg. A thorough physical and neurological examination under anesthesia did not reveal any abnormalities other than those noted previously. Based on the hypermetria, head tilt and slight head tremor the lesion was localized primarily in the cerebellum. However, since signs did not point to a focal cerebellar lession, and because other cerebral signs, including dementia, depression and weakness also were present, a more diffused disease process was suspected.

A complete blood count revealed leukocytosis (white blood cell count of $19.4 \times 10^3/\mu L$; normal range $5.5–15.7 \times 10^3/\mu L$) with neutrophilia (93%) and lymphopenia (6%). Blood chemistry revealed an elevation in total protein levels (9.5 g/dl; normal range 5.4–7.2 g/dl) due to hyperglobuli-

nemia (5.6 g/dl; normal range 2.1–3.5 g/dl). An infectious disease was suspected, based on the findings of leukocytosis and hyperglobulinemia. Possible infectious agents included feline corona virus, *Toxoplasma gondii, Listeria monocytogenes* and *Mycoplasma* spp. While the leukocytosis and differential count also were suggestive of a stress leukogram, it was decided to initiate antibiotic treatment because of the concurrent hyperglobulinemia. The animal was treated with an intramuscular injection of enrofloxacin (Mobay Corporation, Shawnee, Kansas, USA) (250 mg, once a day). No improvement was noted, and treatment was stopped 5 days later. Over the next month, the lioness' condition deteriorated progressively. The hypermetria and right head tilt were noticeably more severe. Several episodes of head pressing and opisthotonos were noted, providing further evidence for a process involving the cerebrum. However, based on the lioness' reaction to foreign objects introduced to its cage, the animal still appeared to have normal cranial reflexes and normal vision.

The lioness was released in a large, fenced park with the rest of the pride. Intramuscular steroid treatment of prednisolone (Upjohn Veterinary Products, Kalamazoo, Michigan, USA) (1 mg/kg, once a day) was administered for 5 days, but no improvement was noticed. The animal's neurological status gradually deteriorated, and 2 mo later a cerebrospinal fluid tap was attempted. No fluid could be collected from the cisterna magna. A complete blood count conducted at this time revealed no abnormalities. Blood chemistry revealed, once again, hyperproteinemia (9.0 g/dl) and hyperglobulinemia (5.2 g/dl). At this stage a developmental abnormality was suspected based on the age of the onset of clinical signs, the gradual deterioration and the lack of response to anti-infective and anti-inflammatory treatment. Our inability to collect a sample of cerebrospinal fluid, and the persistence of signs despite the normal blood count also pointed to a developmental abnormality. The animal died 2 wk later, at the age of 9 mo, 6 mo after the first clinical abnormality was noticed.

FIGURE 1. Median longitudinal section of the brain of a 9-mo-old African lioness with Arnold-Chiari malformation demonstrating herniation of the cerebellar vermis (arrow) into the foramen magnum.

At necropsy the animal's carcass was in normal body condition and no abnormalities were observed in visceral organs. Exploration of the dorsal skin and examination of the spinal cord did not reveal any morphological changes. The internal cranial vault was somewhat flat. The occipital bone was irregularly thickened and platybasic. The cerebellum was reduced in size; the vermis and part of the paravermis were herniated as tonguelike processes into the foramen magnum and the upper cervical spinal canal at the level of C1 (Figs. 1, 2). The medulla was compressed and also

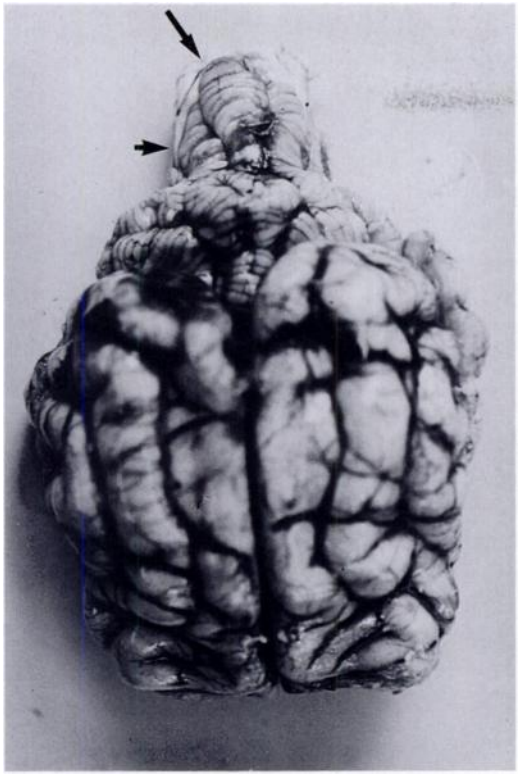

FIGURE 2. Dorsal view of the brain of a 9-mo-old African lioness with Arnold-Chiari malformation demonstrating herniation of the cerebellar vermis (long arrow) and part of the tonsils of the cerebellar hemispheres (short arrow) into the foramen magnum.

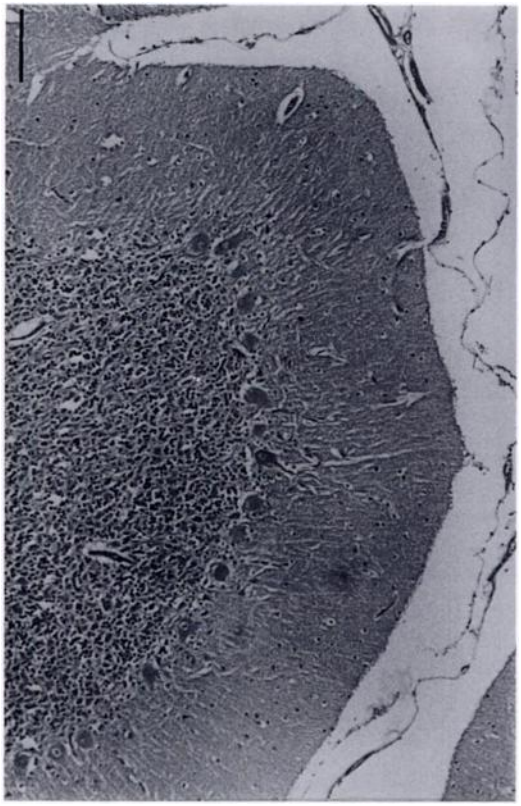

FIGURE 3. Longitudinal section through a non-compressed folium of herniated part of the cerebellar vermis in a 9-mo-old African lioness with Arnold-Chiari malformation. H & E. Bar = 150 μm.

slightly displaced caudally together with the cranial nerves. The thickness of the cerebral cortex near the caudal poles of the occipital lobes was reduced and both lateral ventricles were slightly dilated, indicating the possible presence of internal hydrocephalus. There was no visible enlargement of the foramen magnum, but the cranial cavity of the caudal fossa was somewhat small.

Tissues were fixed in 10% neutral buffered formalin, processed routinely, sectioned, and stained with hematoxylin and eosin (H&E). Microscopic examination of the brain supported the gross postmortem diagnosis. The folia, especially in herniated part of the vermis, were hypoplastic and sometimes dysplastic. There were varying degrees of loss of granule and Purkinje cells (Figs. 3, 4). In the most severely affected folia, the boundaries of each layer were blurred and degenerated Purkinje cells were often present. A marked reduction in the number of neurons in the medullary nuclei (nucleus ambiguus, nucleus olivaris and nucleus dorsalis nervi vagi), as well as swelling of axons in these nuclei, was recorded. Immunoperoxidase staining using panleukopenia and canine distemper antisera was negative. Clinical and necropsy findings were consistent with a diagnosis of Arnold-Chiari malformation in this lion cub.

Arnold-Chiari malformation is described extensively in the human literature, but it is infrequently diagnosed in veterinary medicine. Based on the number of reports, the malformation appears to be most common in domestic cattle (Madarame et al., 1993). Individual cases also

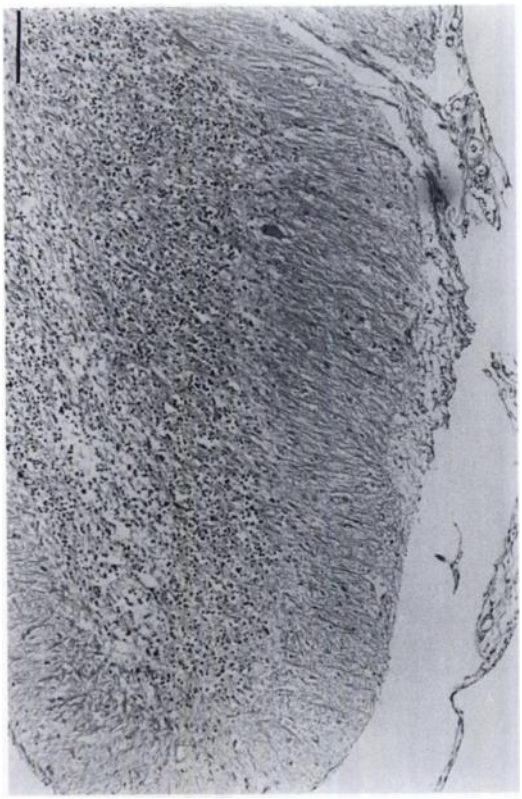

FIGURE 4. Longitudinal section through a compressed folium of herniated part of the cerebellar vermis of a 9-mo-old female African lion with Arnold-Chiari malformation showing depleteion of the granular layer cells and loss of Purkinje cells in the compressed section. H & E. Bar = 150 μm.

have been described in a baboon (*Papio hamadryas*) (Cameron and Hill, 1955), a sheep and a pig (Jubb et al., 1985). There is one brief mention of the malformation in a litter of lions; however, that report does not describe the clinical progression of symptoms in affected cubs (Pappendick et al., 1995). The brief clinical and pathological description resembles the one presented in this report, but the disease was not allowed to progress and the lions were euthanized (Pappendick et al., 1995).

Arnold-Chiari malformation consists of the herniation of tongue-like processes of cerebellar tissue through the foramen magnum into the anterior cervical spinal canal, with caudal displacement and elongation of the medulla oblongata, pons, and the fourth ventricle (Jubb et al., 1996). The Arnold component of the abnormality is the herniation of the cerebellar tissue and medulla; the caudal migration of the pons and medulla is defined as the Chiari component (Innes and Saunders, 1962). The pathogenesis of this malformation is unclear. Examination of affected individuals reveals that the posterior fossa, and perhaps also the anterior fossa, is too small to contain the normal volume of brain tissue (Graham and Lanton, 1996). It has been suggested that a small fossa may result from a failure of neurogenic induction of osseous growth (Jubb et al., 1996). In cattle the anomaly is invariably associated with bilateral elongation of the occipital lobes (Summers et al., 1994). Other accompanying deformities, including spina bifida and meningomyelocele also are noted commonly in animals (Jubb et al., 1996). None of these changes were found in the case described in this report.

Arnold-Chiari malformation was first defined in 1891 by Chiari, who described three types of cerebellar deformities associated with hydrocephalus (Innes and Saunders, 1962; Peach, 1965b). Arnold-Chiari is an encompassing name given to all three types. Chiari type 1 malformation describes a cerebellar herniation restricted to the area of the paravermis. The herniated and elongated paravermis may be histologically normal, or they may be atrophic, infarcted or sclerotic and connected with fibrous tissue to the dorsal medulla. The medulla of individuals with Chiari type 1 malformation is either unchanged or flattened by the herniated cerebellar tissue. This type of malformation has not been associated with spina bifida, but it can be the cause of late onset hydrocephalus (Peach and Bradford, 1965a). Chiari type 1 malformation cases present with a variety of clinical signs which are usually not severe, and the onset of which may be delayed till adulthood.

Chiari type 2 malformation is characterized by elongation of the inferior vermis and brain stem, and their displacement

into the cervical spinal canal. The extent of herniated cerebellar tissue varies in size. The elongated tongue of cerebellar vermis, often in association with the choroid plexus, lies on the dorsal aspect of the medulla and spinal cord (Summers et al., 1994; Peach, 1965b). Spina bifida is almost invariably present in humans with type 2 malformation, and also has been reported in calves (Jubb et al., 1996). Chiari type 3 malformation is very rare. It is found in individuals with occipitocervical or high cervical bony defect; the cerebellum herniates through this bony defect.

The pathogenesis of type 3 malformation is unclear, as none of the existing hypothesis stands up to critical examination (Peach, 1965a). Indeed, researchers are attempting to find an encompassing mechanism that would explain the morphogenesis of the various types of Arnold-Chiari malformations and their associated nervous system anomalies. It is now believed that the pathogenesis of idiopathic syringomyelia, Chiari malformation and bony occipital dysplasia are all closely linked (Schady et al., 1987). It has been suggested that the malformation and related anomalies are the result of developmental arrest occurring during organogenesis (Peach, 1965a). A significant difference in skull shape has been found between human victims of idiopathic adult Chiari type 1 malformation and controls (Schady et al., 1987). The neurological anomalies are considered to be secondary to the skeletal defects (Graham and Lanton, 1996). Compression of the developing medulla within a small posterior fossa causes the abnormalities of the pontine and cervical flexures, while the relatively late growth spurt of the cerebellum means that the cerebellum grows into the spinal canal, rather than being pushed or pulled into it (Graham and Lanton, 1996).

In our case, herniation of the cerebellar vermis and paravermis and the slight caudal displacement of the medulla, combined with lack of displacement in other parts of the brainstem indicate that this case most closely resembles a Chiari type 2 malformation, despite the lack of any spinal cord abnormality. The skull abnormality and the presence of dilated lateral ventricles lends support to the theory that the herniation is secondary to the skeletal defect and that some degree of hydrocephalus is a result of the herniation, rather than its cause (McLone and Knepper, 1989).

In humans, the Arnold-Chiari malformation is known to produce variable clinical signs and symptoms of cerebellar, cervical and/or brainstem dysfunction. Clinical signs reported include obstructive sleep apnea (Dohery et al., 1995), changes in heart rate due to alternation in the medullary autonomic centers (Ireland et al., 1996), disturbances in central regulation of arterial pressure (Arcaya et al., 1993), recurrent syncope (Weig et al., 1991) and head aches. Some patients remain asymptomatic till old age (Arcaya et al., 1993; Dohery et al., 1995; Ireland et al., 1996). Animals are usually affected more severely and do not survive the first year of their lives (Madarame et al., 1993). However, it is possible that moderate cases of Arnold-Chiari in animals are misdiagnosed due to the more obscure clinical signs. We recommend adding this malformation to the list of differential diagnosis for clinical signs that are attributed to cerebellar, cervical or brainstem dysfunction in young lions as well as in other species.

LITERATURE CITED

ARCAYA, J., J. CACHO, F. DEL CAMPO, J. GRANDEM, AND A. MAILLO. 1993. Arnold-Chiari malformation associated with sleep apnea and central dysregulation of arterial pressure. Acta Neurologica Scandinavia 88: 224–226.

CAMERON, A. H., AND W. C. O. HILL. 1955. The Arnold-Chiari malformation in a sacred baboon (*Papio hamadryas*). Journal of Pathological Bacteriology 70: 552–554.

DOHERTY, M. J., D. P. S. SPENCE, C. YOUNG, AND P. M. A. CALVERLEY. 1995. Obstructive sleep apnoea with Arnold-Chiari malformation. Thorax 50: 690–691.

GRAHAM, D. I., AND P. L. LANTON. 1996. Green-

field's neuropathology. Edward Arnold, London, UK, 632 pp.

JUBB, K. V. F., P. C. KENNEDY, AND N. PALMER. 1985. Pathology of domestic animals, 3rd ed. Academic Press, San Diego, California, 574 pp.

———, ———, AND ———. 1996. Pathology of domestic animals, 4th ed. Academic Press, San Diego, California, 780 pp.

INNES, J. R. M., AND L. Z. SAUNDERS. 1962. Comparative neuropathology. Academic Press, New York, New York, 839 pp.

IRELAND, P. D., D. MICKELSEN, T. G. RODENHOUSE, R. S. BAKOS, AND B. GOLDSTEIN. 1996. Evaluation of the autonomic cardiovascular response in Arnold-Chiari deformities and cough syncope syndrome. Archives of Neurology 53: 526–531.

MADARAME, H., N. ITO, AND S. TAKAI. 1993. Dicephalus, Arnold-Chiari malformation and spina bifida in a Japanese black calf. Journal of Veterinary Medicine 40: 155–160.

MCCLONE, D. G., AND P. A. KNEPPER. 1989. The cause of Chiari II malformation: A unified theory. Pediatric Neuroscience 15: 1–12.

PAPENDICK, R., J. SCHUMACHER, AND P. WOLLENMAN. 1995. Arnold-Chiari-like malformation in a litter of lion cubs. Veterinary Pathology 32: 578.

PEACH, B. 1965a. The Arnold-Chiari malformation: Morphogenesis. Archives of Neurology 12: 527–534.

———. 1965b. The Arnold-Chiari malformation: Anatomic features of 20 cases. Archives of Neurology 12: 613–621.

SCHADY, W, R. A. METCALFE, AND P. BUTLER. 1987. The incidence of craniocervical bony anomalies in the adult Chiari malformation. Journal of the Neurological Sciences 82: 193–203.

SUMMERS, B. A., J. F. CUMMINGS, AND A. DE LAHUNTA. 1994. Veterinary neuropathology. Mosby Year Book, St. Louis, Missouri, 527 pp.

WEIG, S. G., P. E. BUCKTHAL, S. K. CHOI, AND R. T. ZELLEM. 1991. Recurrent syncope as the presenting symptom of Arnold-Chiari malformation. Neurology 41: 1673–1674.

Received for publication 30 September 1997.