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CHAPTER 61

# Stargazing in Lions

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Stargazing and related neurologic signs in lions is a well-known syndrome. The name of the disease relates to the characteristic attitude with the lion's head pulled backward, giving the impression that the animal is staring at the sky. It is understood that the proliferation of cranial bones with resulting compression of brain tissue, cause this clinical presentation. Recent reports have been limited to young and adolescent captive African lions *(Panthera leo)* and hypovitaminosis A has been proposed as the cause. There is no gender predilection. Interestingly, there are no reports in Asian lions and there are only rare historical reports of the condition in a 10-month-old tiger *(Panthera tigris)*[6] and in leopards.[8] It has to be clarified that stargazing is only one of a variety of neurologic signs of a vestibular disorder. The description is misleading and is not diagnostic for the syndrome. In most cases, stargazing was not even reported. It may also be discrete, absent, or hidden by other neurologic symptoms. Different terms are used for the same condition, such as *Chiari I–like malformation* or *cerebellar herniation*.* Arnold-Chiari malformation in humans and calves is almost always associated with spina bifida and/or a protruding meningomyelocele. These features were not found in affected lions and therefore we suggest to use the term with caution or to describe it as an Arnold-Chiari–like disorder when discussing the stargazing syndrome of lions.[4]

This chapter summarizes the current state of knowledge regarding pathogenesis, diagnosis, treatment, and prevention of the disease. Clinical observations and pathology are based on a recent case that we diagnosed, which is compared with relevant literature reports.

*References 1, 3, 10, 12, 15, and 19.

## CLINICAL SIGNS

In recent cases, clinical signs were first observed in subadult lions at the age of 9 to 14 months. However, in rare cases, signs were already detected at the age of 2 months. Early detection of clinical signs is important because prognosis seems to be better at the beginning of the growing phase, when bone formation is more dynamic and may respond to therapy. Various occurrence histories have been reported in the literature, such as littermates of affected individuals that grew up normally, or whole litters affected to a higher or lesser extent, or with varying ages at the beginning. In the case that we diagnosed, the female (lion no. 1) of a litter of two was affected, with the first signs observed at the age of 12 months, whereas the male littermate (lion no. 2) grew up normally. A variety of neurologic signs, in most cases a combination of two to five signs, were reported. The signs may be summarized as the neuroanatomic expression of a peripheral or central vestibular disorder. Slow progression of the signs over weeks is a consistent feature. It is recommended to perform repeated video recording of the affected animal to allow for follow-up. This may also serve as a basis for discussion for the neurologist and helps locate the origin of the signs within the central or peripheral nervous system.

Initial signs include ataxia, lack of coordination, and difficulties in negotiating obstacles. Our first observation of signs in the affected lion was the sudden difficulty in jumping through a gate that had a 50-cm step, which connects the indoor and the outdoor enclosure. The animal fell back and it took a second attempt to cross this barrier finally. During the course of the disease, the affected animal eats and drinks normally, but takes smaller quantities, and therefore often appears smaller than other nonaffected members of the litter. Later, progressive ataxia, mild head tilt and cycling behavior (both

often reported as left-sided), stargazing, nystagmus, fine head tremor, staring glare, and nonresponsiveness to new objects (neither playing nor defense behavior) are observed. At this stage, the affected lion often becomes lethargic and depressed. We observed that the ataxic signs worsened when the animal was excited, such as when the animal was separated from the group or when blow-darted. In single cases, abnormal vocalization, hypersalivation, and tongue protrusion were reported. We were able to test pupillary light reflexes, using a pocket lamp at a few centimeters' distance through the cage bars, and obtained a normal response. Late signs of the disease include blindness, convulsions, inability to stand, rolling over, recumbency, and death.*

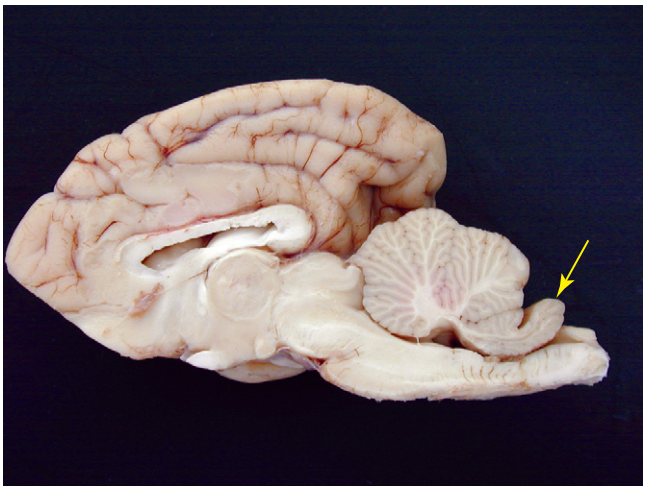

Figure 61-1

CT scan, sagittal view, showing the thickened tentorium cerebelli and occipital bones *(arrow)*. *(Courtesy Institute for Forensic Medicine, University of Bern, Switzerland.)*

## DIAGNOSIS AND DIFFERENTIAL DIAGNOSES

After careful evaluation of the clinical symptoms, the neuroanatomic localization should be investigated. It is important to plan the diagnostic procedures carefully that will be performed during general anesthesia. A complete physical and neurologic examination, including blood and cerebrospinal fluid sampling, should be performed, taking samples for virology, microbiology, and parasitology, carrying out an examination with an otoscope, and having imaging techniques prepared (radiography, ultrasound) or organized (e.g., computed tomography [CT], magnetic resonance imaging [MRI]). Several differential diagnoses have to be considered and a rule-out protocol should be determined for trauma, infection (e.g., feline coronavirus, feline immunodeficiency virus, canine distemper), otitis media and/or interna, or a space-occupying process that compromises the central nervous system (e.g., hematoma, abscess, neoplasia, pathologic bone proliferation, congenital anomaly).

A complete feline hematology and serum chemistry panel, determination of serum vitamin A concentration, feline leukemia virus and feline coronavirus serology, and feline immunodeficiency virus (FIV) Western blot test should be carried out. Serology for *Toxoplasma gondii*, *Ehrlichia canis*, Lyme disease, and Rocky Mountain spotted fever antibodies may be added. Cerebrospinal fluid examination includes cell count and differentiation, protein determination, and polymerase chain reaction (PCR) assay for canine distemper. Ultrasound-guided liver biopsy may be used to measure hepatic vitamin A concentration. Although reference ranges for serum or hepatic vitamin A concentrations have not been established for lions, they may be compared with values of most carnivores, including those of domestic cats. A detailed discussion on serum vitamin A concentrations in lions is presented in the next section of this chapter. Postmortem hepatic vitamin A concentration of the case that we observed was 0.34 µg/g. This is far lower than the hepatic vitamin A concentration of a single wild lion of 6075 µg/g, or references from two earlier postmortem samples from our zoo, 4060 µg/g and 907 µg/g, respectively.

For the detection of pathologic cranial bone thickening, specifically of the os tentorium cerebelli (Fig. 61-1), CT investigation is necessary. Both plain and contrast medium scans are useful. Alterations of brain tissue, such as the compression of the cerebellum, including herniation of the caudal folia through the foramen magnum occipitalis, is diagnostic for the syndrome and best visualized using sagittal MRI scans (Fig. 61-2). An objective interpretation of osseous cranial structures may be achieved by measuring the maximum diameter of the vitreous body of the eye and relating it to the thickest part of the occipital bone and os tentorium cerebelli.[7] Hyperintensity of sagittal images in the spinal cord consistent with syringohydromyelia and secondary enlargement of the lateral ventricles caused by stasis of cerebrospinal fluid were additional MRI findings in recent reports.[10,20]

*References 1-3, 7, 9-11, 15, 16, 19, and 20.

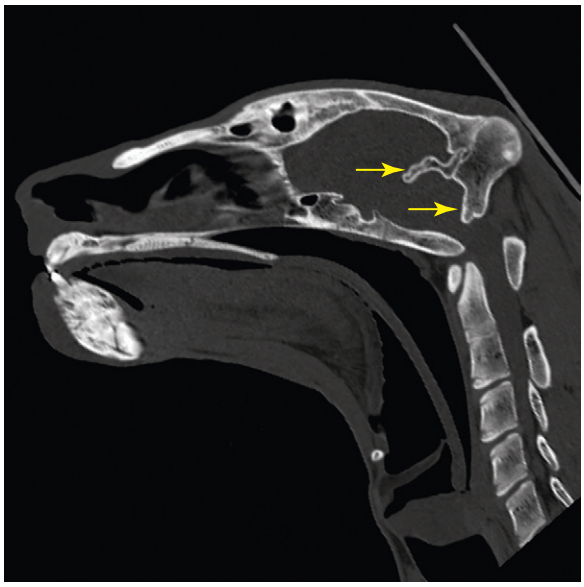

Figure 61-2

Sagittal MRI scan showing compression of the cerebellum, with herniation of the caudal cerebellar folia through the foramen magnum occipitalis *(top arrow)*. The hyperintense area in the cervical spinal cord indicates syringomyelia *(bottom arrow)*. *(Courtesy Institute for Forensic Medicine, University of Bern, Switzerland.)*

## SERUM VITAMIN A CONCENTRATIONS IN LIONS

The accuracy of serum vitamin A (retinol) concentration certainly is lower than the value of the concentration in the liver, which is the reservoir organ for vitamin A. However, tissue analysis is impractical for routine clinical application in zoo animals and therefore serum values may serve as controls for vitamin A status or support a diagnosis of vitamin A deficiency. Table 61-1 shows the serum retinol concentrations of an affected lion cub (lion no. 1) before and after the appearance of the first clinical signs and before and after therapeutic supplementation. The results are compared with the concentrations from nonaffected pack mates and littermates, as well as individual concentrations from subadult free-ranging lions at capture and later as adults in captivity. Finally, serum samples from subadult and adult captive lions from the same zoo and from four other institutions referenced in the literature have been summarized as mean values.[5] Lion no. 1, which developed clinical signs of stargazing at the age of 12 months, showed the lowest serum retinol concentration at that time (37.4 µg/liter). This finding was confirmed by extremely low liver vitamin A values at necropsy (0.34 µg/g). Its littermate, lion no. 2, raised under identical conditions, had a serum retinol concentration (122 µg/liter) that was approximately three times higher. Therefore, an individual problem, such as a congenital deficiency of specific lipoproteins, which are needed for endogenous vitamin A transport, may be theorized. After repeated parenteral vitamin A supplementation, lion no. 1 showed only a slightly increased retinol concentration (60.1 µg/liter), which indicates that the influence of parenteral vitamin A supplementation is limited in the short term. When compared with the reference values from the same institution before 1998, all concentrations measured in the current lion pack (nos. 1 to 4, 6, and 7) were low. Concentrations of free-ranging subadult lions at capture (nos. 3 to 5), which reflected true reference values from the natural availability of whole-prey diets, were also low when compared with those concentrations at the same zoo and four other zoos. They may reflect long-term vitamin A supplementation in a captive situation. We have concluded that serum retinol concentrations below 60 µg/liter are critical for the development of stargazing in growing lions, and values higher than 90 µg/liter are adequate and should be achieved by dietary measures in captivity.

## CAUSE AND PATHOGENESIS

Although the stargazing syndrome in lions has been known for a long time, with the first cases described in two young lions with paraplegia, head tilts, and tremor,[17] the exact cause is still uncertain. The disease was first ascribed to vitamin B deficiency.[14] Later, the hypothesis of a lack of vitamin A was proposed, based on the empirical and experimental data obtained from puppies, calves, and pigs, although the effects of vitamin A on bone metabolism is incompletely understood. It has been suggested that the bony changes result from low vitamin A stores during growth and may not be seen when hypovitaminosis A occurs later in life. A dam with deficient vitamin A will have vitamin A–deficient milk, which may predispose her young to this syndrome. Vitamin A is reported to stimulate the activity of osteoclasts via an unknown mechanism, causing them to increase their acid phosphatase content and resorb bone. The underlying skeletal abnormality involves defective remodeling of membranous bone—development of bone tissue within connective tissue, as in the skull—presumably caused by the stimulatory effect of vitamin A on osteoclastic activity. In the cranium of vitamin A–deficient animals, there is inadequate resorption of endosteal bone, and consequently

**TABLE 61-1** Serum Vitamin A Levels of Free-Ranging and Captive Lions at the Basel Zoo*

| Lion | Age | Vitamin A (μg/liter) | Remarks |
|---|---|---|---|
| No. 1, female, captive-born, Basel Zoo | 6 mo | 57.6 | Radiographic lameness |
| | 6.5 mo | 40.4 | Radiographic lameness |
| Developed ataxia within 12 mo | 12 mo | 37.4 | Stargazing MRI scan |
| | 13 mo | 60.1 | Euthanasia after 1 mo of parenteral vitamin A supplementation; liver vitamin A level at necropsy = 0.34 μg/g |
| No. 2, male (littermate of no. 1), captive-born, Basel Zoo | 14 mo | 122.0 | Checkup |
| No. 3, female (mother of no. 1 and 2) | | | |
| Free-ranging† | 10 mo‡ | 96.2 | Sample taken at capture |
| Captive-born, Basel Zoo | 5.5 yr‡ | 122.4 | Implant for contraception |
| No. 4, female | | | |
| Free-ranging† | 14 mo‡ | 109.0 | Sample taken at capture |
| Captive-born, Basel Zoo | 6 yr‡ | 54.2 | Implant for contraception |
| No. 5, male, free-ranging | 11 mo‡ | 93.5 | Sample taken at capture |
| No. 6, male, captive-born, Basel Zoo | 18 mo | 61.6 | Crating for transfer |
| No. 7, female, captive-born, Basel Zoo | 18 mo | 62.6 | Crating for transfer |
| Values from 15 subadult and adult captive lions, Basel Zoo, 1987-1998 (mean ± SD) | | 163.8 ± 31.75 | Miscellaneous immobilizations |
| Values from 14 lions, 1-17 yr old, from four U.S. zoos (mean ± SD)[5] | | 130.0 ± 33.0 | |

**Compared with reference levels from the Basel Zoo and four other zoos.*
*†National Park, South Africa.*
*‡Age estimated.*

there is an asynchrony between the developing central nervous system (CNS) and the bones of the skull and spinal column, causing secondary changes in the CNS, with a variety of nervous signs. In the cranium, the defect is particularly severe in the bones of the caudal fossa and the cerebellum may herniate into the foramen magnum. In puppies with vitamin A deficiency, deafness is a prominent sign because of changes in the internal auditory meatus, whereas affected calves and pigs develop blindness caused by narrowing of the optic foramina and compression of the optic nerves. However, deafness has never been reported in affected lions and blindness only rarely. The basis for these variations among species is unclear, but the lesions are modified according to the severity of the deficiency and the stage of skeletal growth. Membranous bones in other locations, including the periosteal surface of the long bones, may also be affected and develop a coarse profile, but endochondral bone, as in the growth of the length of long bones, with gradual replacement of cartilage by bone tissue, does not appear to be directly influenced by vitamin A deficiency. Another proposed mechanism causing clinical nervous signs might be related to hydrocephalus mainly caused by impaired absorption of cerebrospinal fluid into the blood, a process that occurs in the arachnoid villi. The villi are located in the tentorium cerebelli, which is affected by the thickening that occurs in the dura mater in vitamin A deficiency. Hypersecretion of cerebrospinal fluid also contributes to the development of hydrocephalus.[18] This hypothesis, based on vitamin A deficiency, has been reinforced by the fact that improvement and resolution of signs were achieved in young cubs through parenteral vitamin A supplementation.[7]

This vitamin A assumption was, however, refuted in a study done on 149 cases of affected lions and leopards in France.[8] The clinical signs appeared between day 1 and 2 years after birth, with a maximum peak between 3 and 10 months. In all cases, herniation of the cerebellar vermis through the foramen magnum was observed, but thickening of the occipital bone was present in only 50% of cases, contrary to the theory of a primary osseous lesion. Furthermore, similar cerebellar herniation was also observed in fetuses and in healthy adult lions. A

pedigree analysis has failed to show a primary genetic problem, but an infectious viral cause has been proposed based on epidemiologic considerations and the observation of cytopathogenic effect on cell cultures from affected animals.

## TREATMENT

Therapeutic measures include conservative and surgical treatment or a combination of both. Glucocorticoids are used to reduce the swelling or edema of brain tissue and neurologic signs may improve because of decompression and pain relief. The typical initial dose of dexamethasone is 2 to 3 mg/kg/day, which may later be reduced to 0.2 mg/kg/day. Alternatively, prednisone was used at a dosage of 1 mg/kg/day for 3 weeks, which was later reduced by 50%.[16] In addition, vitamin A should be administered. Reported dosages vary from 2000 IU/kg/wk IM for 4 weeks and then every 2 weeks for four more doses,[7] up to 5000 IU/kg/daily PO, until full adult size is reached.[10] It is recommended to start with a parenteral application because a disorder of enteral absorption of vitamin A may be present. Hartley and colleagues[7] have reported that all of the seven mildly affected cubs showed some improvement within 2 weeks and all clinical signs had disappeared after 3 months, using only vitamin A supplementation. The beneficial effect of conservative treatment was also initially reported in other cases. However, in most reports, there was consistent recurrence of neurologic signs and further deterioration. It is assumed that younger and/or mildly affected animals at an age when the cranial bones start to grow fast may respond better to a conservative approach. Recently, successful suboccipital craniectomy and laminectomy were performed in two cases to achieve surgical decompression of the caudal fossa, and the clinical signs disappeared quickly.[10,16] Surgical decompression, together with adequate preoperative and postoperative medical care, may be the only way to cure this condition. Individuals in an advanced state of disease should be euthanized immediately for animal-welfare reasons and submitted for postmortem examination.

## NECROPSY AND HISTOPATHOLOGY

The most obvious lesion reported in all cases of lions with similar signs is the severe thickening of the osseum tentorium cerebelli and of the occipital bone, leading to crowding of the caudal fossa and subsequent herniation of caudal cerebellar folia through the foramen magnum occipitalis (Fig. 61-3). Closer inspection of the skull reveals increased thickness of all bones composing the brain case as well as thickened mandibular bones. Dilation of the lateral ventricles, as well as syringomyelia of the cervical spinal cord have also been observed. A few reports have also described fragile teeth, with thin enamel.*

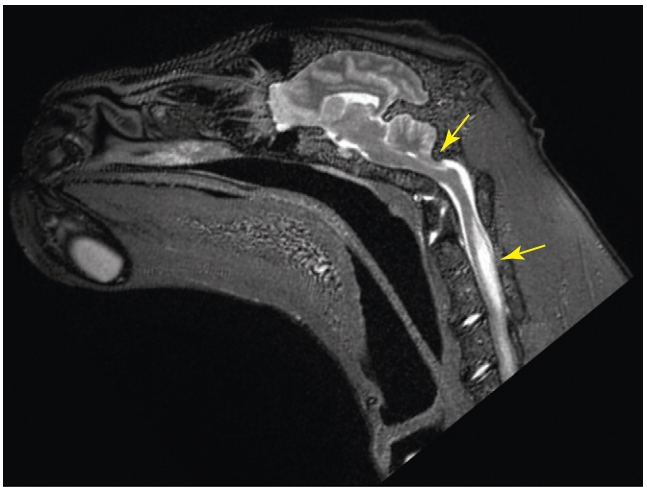

Figure 61-3

Sagittal midline section of the brain showing the herniated caudal cerebellar folia *(arrows)*.

Histopathologic lesions of the bones are characterized by thickened, poorly remodeled bone tissue caused by a shift from compact to cancellous bone. Examination of the tentorium cerebelli reveals thickening, mostly caused by the growth of new periosteal woven bone containing retained cartilaginous cores. Histologic lesions of the nervous tissue are mostly confined to the herniated cerebellar folia, compressed brainstem, and cervical spinal cord. Cerebellar lesions include thinning and rarefaction of the molecular layer, loss of Purkinje cells, granular cells associated with proliferation of Bergmann's glia, and disseminated punctate hemorrhages. Varying degrees of malacia and wallerian degeneration characterized by dilated myelin sheaths, axonal swelling (spheroids), and digesting chambers associated with astrogliosis may be observed in the white matter of the compressed cerebellar folia, medulla oblongata, and different tracts of the cervical spinal cord. Edema and the formation of syringomyelia are mostly observed in the dorsal tract of the cervical spinal cord. Meningeal lymphoplasmacytic infiltration, fibroplasia, and hemorrhages may also be observed focally in these compressed regions.

*References 1-3, 7, 11-13, 15, 19, and 20.

## PREVENTION

Hypovitaminosis A is assumed to cause the skull bones to become thicker, which is responsible for the cerebellar compression of stargazing lions. Therefore, the diets of captive African lions, especially of growing cubs, need careful veterinary evaluation and supervision of the diet for adequate vitamin A content. Several case reports of stargazing lions have mentioned a history of meat or beef on the bone diets without supplementation. However, other reports have noted daily or weekly multivitamin supplements without indicating exact quantities.

Meat on the bone feeding is the most frequent diet given to the lions in our institution. Every ration includes a mineral and vitamin supplement in powder form containing 91,000 IU/kg of vitamin A. This supplement is added at a dosage of 5% to the total food ration. The keepers were made aware of the need to supplement minerals and vitamins, and were trained to provide sufficient supplementation—for example, by weighing samples, such as 50 g of supplement/kg of food, which is equivalent to 4550 IU vitamin A/kg of food. The powder supplement is applied to deep cuts in the meat, so that it cannot easily fall off. African wild dogs, wolves, snow leopards, cheetahs, and lions, including a healthy littermate of an affected lion, were raised in the zoo in the last decade without any problems and, to the best of our knowledge, there was no change in feeding regimen, technique, or staff. Usually, there are two irregular fasting days per week in the feeding management of the lion group. Additionally, freshly killed whole prey, such as rats, chicken, and hoofstock from the zoo, including their livers, which are rich in vitamin A, are fed at weekly or monthly intervals. Despite all these precautions, a fatal case of a stargazing lion occurred. We therefore find it difficult to believe that a lack of vitamin A intake is the sole cause in this case and other factors must be considered. Pathologic alterations in vitamin A absorption or metabolism have to be considered in individual cases. As opposed to the digestion of herbivores, vitamin A metabolism from carotene is not important because the enzyme carotenase is absent in felids. However, no morphologic signs of endogenous alterations have so far been found in necropsies. Further studies of vitamin A digestion, absorption, and metabolism in lions are required and need to be compared with those made in other felid species.

Practical feeding techniques, such as group feeding and their associated feeding-related social interactions, may be important because, under such conditions, the exact individual intake of supplemented food cannot be determined. Additional preventive measures in addition to supplementation include an increased quantity of whole-prey food or bovine liver on a weekly basis. Daily liver feeding is not recommended because it could result in diarrhea or hypervitaminosis A.

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