Case Report

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Journal of Veterinary Medicine and Surgery
ISSN 2574-2868

2017
Vol. 1 No. 3: 15

DOI: 10.4172/2574-2868.100015

Xanthogranuloma and Hepatic Lipidosis in a Mexican Moccasin Snake (*Agkistrodon bilineatus*) with Hypercholesterolemia: A Case Report

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Abstract

The Xanthogranuloma or granuloma of cholesterol is a degenerative lesion that occurs by a nodular accumulation of cholesterol and other lipids, accompanied by granulomatous inflammation. In reptiles, this is a poorly informed lesion, which has been associated with hyperlipidemia, dietary or hormonal factors and trauma. The aim of this report is to describe a xanthogranuloma in a 13-year-old female snake (*Agkistrodon bilineatus*), referred to the Department of Pathology of the Faculty of Veterinary Medicine and Zootechnics of the National Autonomous University of Mexico (FMVZ-UNAM), for postmortem analysis. The snake was presented with anorexia, depression, head tilt, chronic inflammation and hypercholesterolemia. Hepatic lipidosis and a cholesterol granuloma replacing 60% from the brain were diagnosed. The knowledge of this disease in snakes with neurological signs is important because they can be associated with the cause of death.

Keywords: Xanthogranuloma; Cholesterol granuloma; Hypercholesterolemia; Snake; *Agkistrodon bilineatus*

Received: August 31, 2017; **Accepted:** September 07, 2017; **Published:** September 13, 2017

Citation: Vargas-Soto LM, Vázquez-Briones DB, Núñez-Ochoa L, Reyes-Matute A (2017) Xanthogranuloma and Hepatic Lipidosis in a Mexican Moccasin Snake (*Agkistrodon bilineatus*) with Hypercholesterolemia: A Case Report. J Vet Med Surg. Vol. 1 No. 3: 15.

Case Report

The xanthogranuloma or granuloma of cholesterol is a degenerative lesion that occurs by a nodular accumulation of cholesterol and other lipids, accompanied by granulomatous inflammation (foamy macrophages and multinucleated giant cells). It is considered a consequence of foreign body response to the presence of crystallized cholesterol. This lesion is mainly located in the choroid plexus, lateral ventricles and the fourth ventricle [1,3,7,8]. Xanthogranuloma has been reported in humans, birds, reptiles, amphibians, dogs, cats and more frequently in horses, where it is mainly associated with aging and is usually a finding at necropsy [1,3,4,6-8]. In humans and birds it is commonly a cutaneous disease, [8] in dogs and cats it has been described in middle ear (aural cholesteatoma) [4] and in reptiles it has been anecdotically reported (mostly described in lizards). In lizards it has been associated with hypercholesterolemia in some cases. The [8] aim of this paper is to describe the morphologic and clinical pathology of a Mexican moccasin snake with an intracerebral cholesterol granuloma (CG), with concurrent hypercholesterolemia and hepatic lipidosis.

A 13-yr-old female, Mexican moccasin snake (*Agkistrodon bilineatus*), was presented with a history of anorexia of one month, depression and distortion from the first third of the body due to head tilt. The snake was fed with pre killed mice. Clinical pathology tests were performed at the Clinical Pathology Laboratory at the FMVZ-UNAM, where chronic inflammation (heterophilia 3.4 × 10^9/L, reference interval [RI] 0.03-0.4 × 10^9/L, monocytosis 1.6 × 10^9/L, RI 0.1-1.2 × 10^9/L and hyperglobulinemia 42 g/L, RI 5.1-18.2 g/L), extreme hypercholesterolemia (21 mmol / L, RI 4.17- 4.81 mmol / L), and a glutamate [1,6,8] dehydrogenase (GLDH), of 30 U/L (RI unavailable) were found. Values were obtained for *A. piscivorus*, because the ones for *A. bilineatus* were not available [10]. One week later the snake was found dead at its enclosure. The snake was submitted to the Pathology Department at the FMVZ-UNAM for postmortem study, and

latero-lateral and ventro-dorsal radiographs were performed to rule out vertebral compromise. On gross examination, the snake showed overweight, with great amounts of fat bodies covering all the organs of the middle and caudal coelom. Fifteen milliliters of yellowish translucent material classified as transudate where obtained. The liver was moderately enlarged, with round edges and had a pale brown-yellowish color consistent with hepatic lipidosis **(Figure 1A).** While performing a medial cut of the brain, a cavitation containing a brown to yellowish material occupying and replacing approximately 60% of the brain parenchyma was found, this created a concave depression after removal **(Figure 1B).**

On histopathology, compressing the cerebral parenchyma and replacing approximately 60% of the cranial cavity **(Figure 1C);** there was a well-delineated nodular deposit, of abundant dense amphophilic material, intermixed with cholesterol clefts. This material was surrounded and infiltrated by large amounts of macrophages with finely vacuolated cytoplasm and heterophils **(Figure 2).** Moderate gliosis and satelitosis were observed in the cerebral parenchyma. In the liver, hepatocytes were found to be swollen because of numerous abundant clear vacuoles that displaced the nucleus towards the periphery (lipid degeneration).

The diagnosis of xanthogranuloma secondary to hypercholesterolemia was established based on the correlation of the results of clinical pathology (hypercholesterolemia) and the macroscopic and microscopic findings observed. Case reports and case series in reptiles have conclusively diagnosed xanthomatous lesions in several species of geckos, [6] water dragons, [8] but it has only been diagnosed in three different species of snakes, which include a Long-nosed snake (*Rhinochelius lecontei*), a Gopher snake (*Pituophis catenifer sayi*) and a Russian viper (*Vipera lebetina turanica*) [1,8]. In these snakes lesions were found in the lateral ventricles, skin, and spinal dura respectively. In this case, due to the size of the lesion it was not feasible to determine whether the CG was arising from the choroid plexus or from other location in the parenchyma. According to these reports cerebral xanthogranulomas in reptiles might be infrequent. CG has been sometimes associated with hypercholesterolemia and hypertriglyceridemia, and the severity of xanthoma lesions is often directly related to the degree and duration of hypercholesterolemia [6,8]. In reptiles, the evaluation of lipid metabolism comprises cholesterol and triglycerides, in our facility the reptile panel only includes cholesterol, so triglycerides were not evaluated in this case. In horses, it is suggested that their development at sites of hemorrhage or inflammation, is a consequence of trauma. In lizards [2], it is hypothesized that when they repeatedly hit with an element of their enclosure, they may suffer some hemorrhages and brain contusions, which could predispose to the development of xanthogranulomas in choroid plexuses [8]. In this species of snake, this might be likely due to their aggressive behavior, but there was no evidence of acute or chronic hemorrhage which could be related to trauma. In one of the other reported cases of cerebral CG in a snake, the plasma cholesterol and lipids were not determined, and the snake was reported as emaciated and with almost nonexistent fat bodies. Therefore [1] no direct correlation could be established between the CG and hyperlypidemia. Emaciation has also been described in geckos with CG [8]. Neurological signs reported in reptiles with cerebral xanthomas include opisthotonos, horizontal head movements, torticollis, incoordination, and convulsions. In [6] this case, head tilt was the only clinical sign reported, which is easily explained by the size attained by the CG. In horses, CG seldom produces clinical signs [2], but when they achieve a great size, they can be associated with hydrocephalus and neurological signs. Hydrocephalus has also been described in geckos as a consequence of obstruction [6]. CG has been reported coexisting with meningiomas, where it has been proposed that the inflammation and hemorrhage resulting from the neoplasm

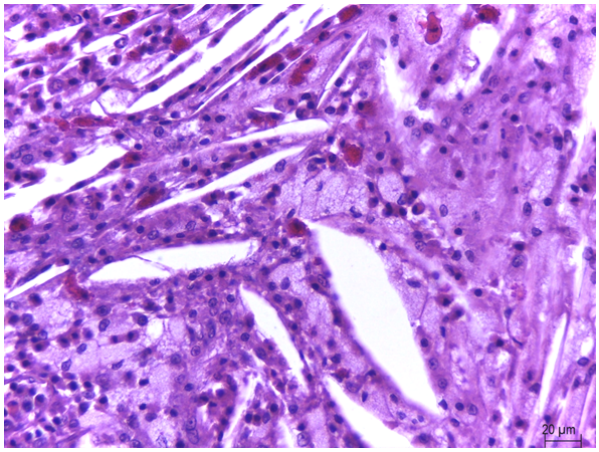

Figure 2 Mexican Moccasin Snake (*Agkistrodon bilineatus*). Microscopically the cholesterol granuloma is composed of acicular cholesterol clefts and surrounded by macrophages, heterophils and scant erythrocytes. Hematoxylin and eosin X40 Bar=20 µm.

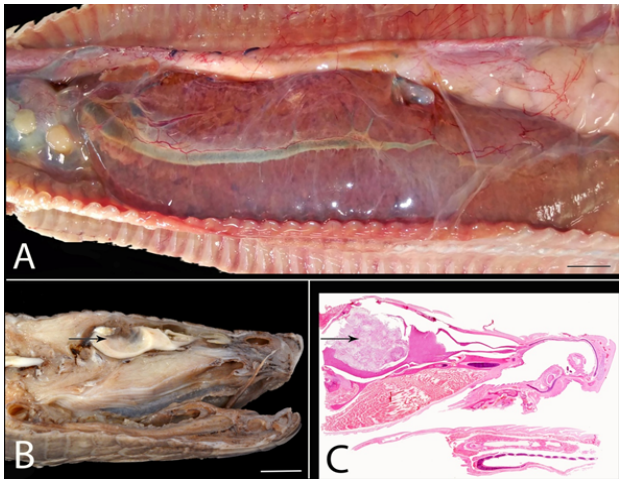

Figure 1 Mexican Moccasin Snake (*Agkistrodon bilineatus*). The liver is swollen and pale brown, which is consistent with hepatic lipidosis. Bar=5 cm. (B) Longitudinal section of head, the brain is partially replaced by a convex depression (arrow), where the cholesterol granuloma was located on (C), this depression is filled by a large, expansible mass of eosinophilic and amorphous material (cholesterol clefts, arrow). Bar=1 cm.

could result in cholesterol crystal deposition and CG formation [4]. In reptiles, hepatic lipidosis may be due to an increase in food consumption, to drug intoxication and in some species it occurs physiologically during hibernation. In females it is common to find accumulation of fat reserves during folliculogenesis, especially in those that do not reproduce [2,5]. The latter could explain why CG has been reported more frequently in females than in males [8]. In this case, hepatic lipidosis was thought to be related with the overweight presented by the animal which was also supported by the great amounts of fat bodies and increased GLDH. Fat deposits in reptiles, as in other animals, may be subcutaneous, intracellomic and parenchymal, such as the liver. An increase in their size is usually seen in obese reptiles. Although no reference values were obtained for GLDH in this species, a value of 30 U/L is considered significant in mammals and birds. Glutamate dehydrogenase is a liver-specific enzyme usually associated with hepatocellular necrosis because it is located within the mitochondria of hepatocytes [9]. The heterophilia and monocytosis presented is consistent with chronic inflammation, [2] which could be related to the inflammation observed surrounding the CG in absence of other sources of inflammation.

Conclusion

Because of the increasing demand of reptiles as pets, it is essential to know the different diseases that these animals suffer. It is essential to perform a comprehensive diagnosis, taking into account clinical history, the presence of neurological signs such as head tilt, opisthotonos, horizontal head movements, torticollis, incoordination and seizures, related to laboratory results such as extreme hypercholesterolemia. There are few reports of xanthogranulomas in reptiles, this lesion has been mostly described in lizards and more frequently in females and no correlation between hypercholesterolemia and the development of xanthogranulomas has been reported in snakes. The knowledge of these lesions in reptiles is important, particularly in obese individuals with nervous signs similar to those described in the present case.

Acknowledgment

The authors thank Jaime Eugenio Cordova López for photography editing

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