

## Synophthalmia in a Holstein cross calf

Hossein Nourani<sup>1\*</sup>, Iraj Karimi<sup>2</sup>, Hossein Rajabi Vardanjani<sup>3</sup>

<sup>1</sup> Department of Pathobiology, Faculty of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran; <sup>2</sup> Department of Pathobiology, Faculty of Veterinary Medicine, Shahrekord University, Shahrekord, Iran; <sup>3</sup> Department of Pharmacology, Faculty of Pharmacy, Student Research Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

### Article Info

#### Article history:

Received: 22 December 2013

Accepted: 27 April 2014

Available online: 15 December 2014

#### Key words:

Craniofacial anomalies

Cyclopia

Holstein calf

Synophthalmia

### Abstract

Synophthalmia is a form of cyclopia, in which some elements of two eyes are fused and form a single eye in the middle region of the forehead. The head of a Holstein female calf born from a 5-year-old cow was referred to Department of Pathology, School of Veterinary Medicine, Shahrekord University due to multiple congenital anomalies. The calf had been slaughtered immediately after birth due to severe respiratory distress by the owner. The calf showed multiple birth defects, including synophthalmia, holoprosencephaly, absence of optic chiasma, hypoplastic maxilla, curved mandibles, arrhinia and dental pad agenesis. A normal tongue protruded from the defect and small oral cavity. To our knowledge, this particular combination of craniofacial defects has not been previously described in Holstein calf.

© 2014 Urmia University. All rights reserved.

### گزارش سین افتالمی در یک راس گوساله هلشتاین

#### چکیده

سین افتالمی یکی از اشکال سیکلوپی می باشد که در آن برخی از ساختارهای دو چشم به یکدیگر متصل شده و یک چشم منفرد را تشکیل می دهند که در ناحیه میانی پیشانی قرار می گیرد. ناحیه سر یک راس گوساله هلشتاین متولد شده از یک گاو ۵ ساله به دلیل وجود ناهنجاری های تکاملی مادرزادی متعدد به بخش پاتولوژی دانشکده دامپزشکی دانشگاه شهر کرد ارجاع داده شد. این گوساله بعد از تولد به دلیل نارسائی شدید تنفسی توسط دامدار ذبح شده بود. ناهنجاری های تکاملی مشاهده شده در گوساله درگیر شامل سین افتالمی، هولوپروزنسفال، فقدان کیاسمای بینایی، هیپوپلازی فک بالا، استخوانهای خمیده فک پایین، تشکیل نشدن ناحیه بینی و عدم تشکیل بالشتک های دندانانی بودند. زبان طبیعی از حفره دهانی کوچک و ناقص بیرون زده بود. بر اساس دانش نویسندگان مقاله، این ترکیب ویژه ناهنجاری های ناحیه سر و صورت در گوساله هلشتاین گزارش نشده است.

**واژه های کلیدی:** سیکلوپی، سین افتالمی، گوساله هلشتاین، ناهنجاری های سر و صورت

#### \*Correspondence:

Hossein Nourani. DVM, PhD

Department of Pathobiology, Faculty of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran.

**E-mail:** nourani@um.ac.ir

## Introduction

Cyclopia is the presence of a single median orbita that contains either a single eyeball, true cyclopia or incompletely fused eyeballs, synophthalmia.<sup>1</sup>

Over 50 years ago scientists demonstrated that holoprosencephaly and the related craniofacial deformities, called 'monkey face lamb disease' were produced in lamb fetuses when pregnant ewes grazed on *Veratrum californicum* early in gestation.<sup>2</sup>

In cow, cyclopia has been reported in a brown swiss cross calf,<sup>1</sup> Friesian calf,<sup>3</sup> German Fleckvieh calf,<sup>4</sup> Hariana breed calf.<sup>5</sup>

To the authors' experiences, this particular combination of craniofacial defects has not been previously described in Holstein calf and this report describes macroscopic characteristics of a unique congenital abnormalities.

## Case Description

The head of a Holstein female calf born from a 5-year-old cow was referred to Department of Pathobiology, School of Veterinary Medicine, Shahrekord University, Iran due to multiple congenital anomalies. There was no record of disease, treatment and suspicious diet in the history of dam. The calf was slaughtered immediately after birth due to severe respiratory distress by the owner. The head was examined grossly and the anomalies recorded.

The most striking malformation was the presence of a single median orbita that contained incompletely fused exophthalmic eyeballs (Figs. 1 and 2). Duplication of anterior intraocular structures, such as lens and pupil were found but there was one optic nerve. The brain was primitive with no cerebral hemispheres (holoprosencephaly) and gray and white matters differentiation (Fig. 3).

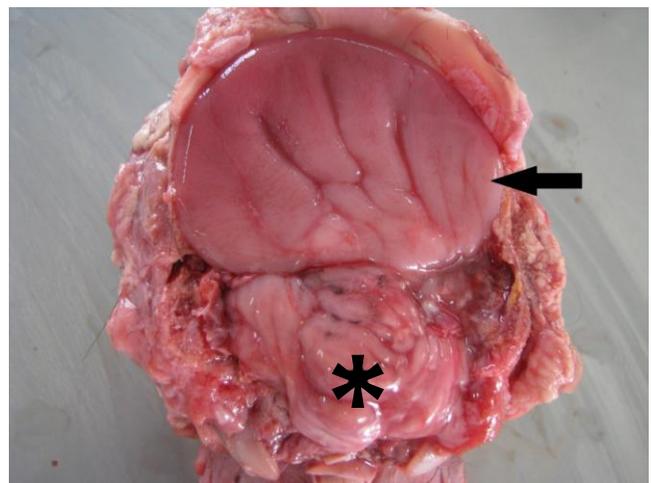


**Fig. 1.** Synophthalmia. A single median orbita (arrow) with incompletely fused exophthalmic eyeballs.

There was no optic chiasma. Other important defects included hypoplastic maxilla, curved mandibles, arrhinia and dental pad agnesis. A normal tongue was protruded from the defect and small oral cavity (Figs. 2 and 4).



**Fig. 2.** Synophthalmia (arrow), arrhinia and protrusion of tongue.



**Fig. 3.** Dorsal view of holoprosencephaly. There are no cerebral hemispheres (arrow), Cerebellum (asterisk).



**Fig. 4.** Lateral view of the head with strongly curved left mandible.

## Discussion

In this case, the possible cause of the craniofacial defects could not be ascertained. In sheep and goat, craniofacial defects such as cyclopia or synophthalmia are caused by ingestion of plants of *Veratrum* species. These anomalies are varied from the extreme malformation, cyclopia to mildly deformed upper jaws.<sup>6</sup>

The toxins of *Veratrum californicum* were shown to be steroidal alkaloids, primarily cyclopamine.<sup>6</sup> Cyclopamine is teratogenic and inhibits the hedgehog (hh) signal transduction pathway. Mouse embryos cultured in the presence of cyclopamine, showed cyclopia and the associated developmental brain defect holoprosencephaly.<sup>7</sup> Cyclopamine-induced malformations in chick embryos are associated with interruption of sonic hedgehog (hh) mediated dorsoventral patterning of the neural tube and somites.<sup>8</sup> Cyclopamine induced cyclopia is reported in rabbit embryos too.<sup>6</sup>

In humans, the synophthalmia is a result of neural plate misdevelopment syndrome involving the eye, brain, skull and face. It is well known that synophthalmia is due to heterogenous causes, most of which to chromosomal abnormalities.<sup>9</sup>

In the present case, nose, upper jaw and the cerebral hemispheres were absent. Similar anomalies have been reported by Minoru and Katsumi, 1999 in three calf cases of cyclopia.<sup>10</sup>

To our knowledge, this particular combination of craniofacial defects has not been previously described in Holstein calf.

## References

1. Ozcan K, Gürbulak K, Takçi I, et al. Atypical cyclopia in a brown swiss cross calf: a case report. *Anat Histol Embryol* 2006; 35: 152-154.
2. Welchl KD, Panter KE, Lee ST, et al. Cyclopamine-induced synophthalmia in sheep: defining a critical window and toxicokinetic evaluation. *J Appl Toxicol* 2009; 29: 414-421.
3. Hammada AK, Abdoud MY. Cyclopia in a Friesian calf. *Egypt J Phytopathol* 1989; 17(1): 76-82.
4. Schulze U, Distl O. Case report: arhinia and cyclopia in a German Fleckvieh calf. *Dtsch Tierarztl Wochenschr* 2006; 113: 236-239.
5. Sharma A, Bhardwaj HR. Atypical cyclopia in a cow calf. *Intas Polivet* 2009; 10(11): 260-261.
6. James LF, Panter KE, Gaffield W, et al. Biomedical applications of poisonous plant research. *J Agric Food Chem* 2004; 52: 3211-3230.
7. Williams DL. Congenital abnormalities in production animals. *Vet Clin Food Anim* 2010; 26: 477-486.
8. Incardona JP, Gaffield W, Kapur RP, et al. The teratogenic *Veratrum* alkaloid cyclopamine inhibits sonic hedgehog signal transduction. *Development* 1998; 125: 3553-3562.
9. Ahn BM, Kim WS, Song MY, et al. A case of synophthalmia with chromosomal anomaly: 46, XX, -15,t(15q,21q). *J Korean Pediatr Soc* 1994; 37: 854-860.
10. Minoru H, Katsumi H. Three calf cases of cyclopia. *J Japan Vet Med Assoc* 1999; 52(10): 644-647.