DIAGNOSTIC EXERCISE

From The Davis-Thompson Foundation*

Case #:**251**; Month: **December**; Year: **2024**

Answer Sheet

Title: Diprosopia in a calf

Contributors: Ariadni Kotzias Bandeira[1], Silvio C. Fonseca[1] and Fábio S. Mendonça[1]
[1]Laboratory of Animal Diagnosis, Federal Rural University of Pernambuco, Recife, PE, Brazil.
Corresponding author: fabio.mendonca@ufrpe.br

Clinical history: A technical visit to a farm was requested due to the birth of a neonate calf with anatomical deformities in its head. The calf was unable to suckle and for this reason, was receiving fresh cow milk in a feeding bottle, but died 3 days after birth.

Gross Images:

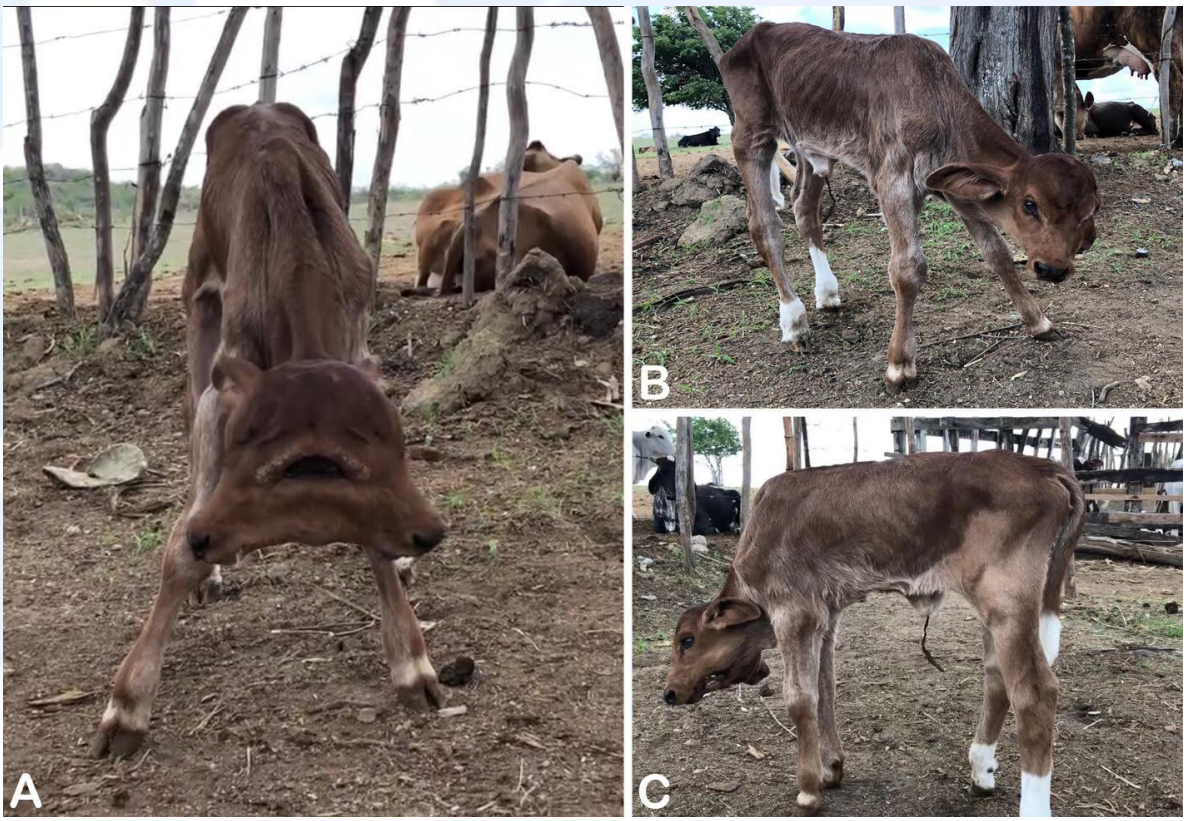

Figure 1.

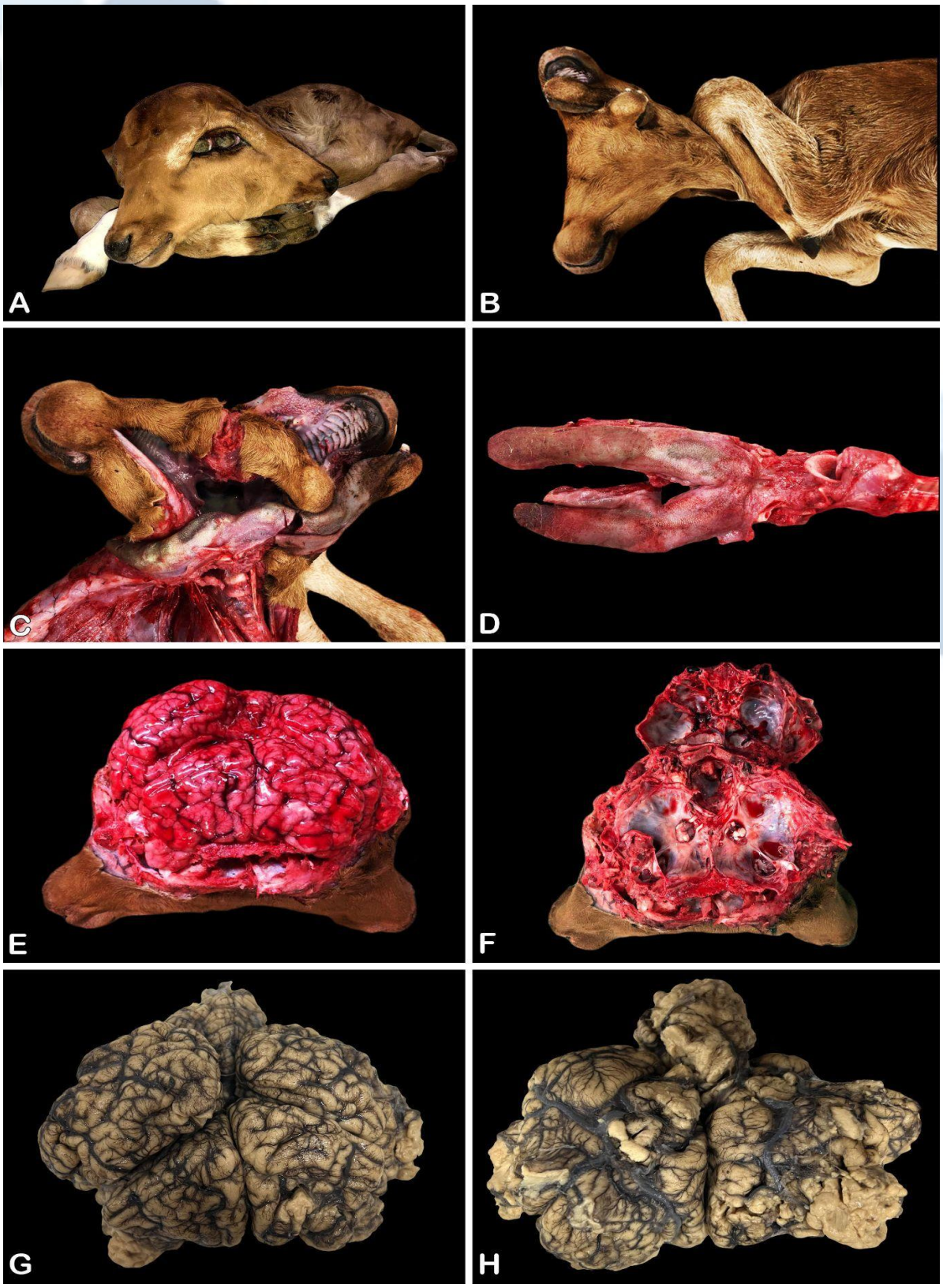

Figure 2

Follow-up questions:

●Macroscopic description
● Name of the condition
● Possible etiologies

Macroscopic description: there is an incomplete craniofacial duplication (complete duplication of the snout) tetraophthalmos with two correctly positioned lateral eyes and an ocular structure located medially between the union of the cranial caps, composed of two partially fused globes (Fig. 1 A-C and 2 A-B). Two anatomically normal ears, located on the right and left regions of the head are observed. There are two oral cavities composed of a maxilla, a mandible and a tongue each, that joined in the caudal region. The mandible of the left face has a lateral deviation, moderate micrognathia and a complete disjunction of the mandibular symphysis, in addition to an irregular number of teeth (Fig. 2 B-D). The naso-oropharynx, larynx, trachea and esophagus are single and no abnormalities are observed. When opening the skull, two caps were observed joined at the height of the frontal, parietal and temporal bones, forming a single cavity, in addition to two *sella turcica*, a brain formed by two forebrains, a single brain stem, and a single cerebellum (Fig. 2E-H).

Name the condition: Incomplete twinning (diprosopia)

Possible etiology: Diprosopia has no defined etiology, but is related to hereditary factors, gene mutations, nutritional factors, viral infections and chemical factors such as ingestion of toxic plants and drugs.

Comments:

Diprosopia is a rare anomaly where the cephalic region and facial structures are duplicated, which may occur completely or incompletely. When in complete state, also referred to as dicephaly, the duplicated structures are entirely separate and the two vertebral axes are separated and parallel. In an incomplete duplication, the duplicated structures remain attached, often presenting a monomorphic pattern, with only the duplicated face being noticeable and despite there being a single vertebral column, there are two complete vertebral axes within (3, 1).

It is thought that the pathophysiology of diprosopia involves the rostral bifurcation or forking of the notochord, which results in the production of two neural plates and their neural crest descendants as well as two side-by-side orientated vertebral axis (1).

Diprosopia has no defined etiology, but is also related to hereditary factors, defects in germ cell genes and environmental factors that interfere with embryonic development. Diprosopia may be an oligogenic inheritance, since it is not observed in parents and ancestors and has a low occurrence in the herd. Therefore, it could be avoided by reducing inbreeding and eliminating parents with a history of producing offspring with this anomaly (10). The connection between genetics and congenital malformations is difficult to establish, mainly due to the variety of phenotypic manifestations, which often appear unrelated and vary among affected individuals. Studies suggest that the development of malformations often involves the interaction of multiple genes and their influence by the environment. In some cases, the

determination may be monogenic, and the various phenotypic manifestations may result from pleiotropic effects of a single gene (8).

In humans, diprosopia can be caused by changes in the SHH (Sonic HedgeHog Homolog) protein and its corresponding gene as they are fundamental in signaling the craniofacial pattern. Its excess leads to duplication of facial structures and an insufficient amount of the protein leads to insufficiently developed facial features (4).

Toxic plants belonging to the genus Veratrum, Lupinus, Astragalus, Oxytropis, and Conium represents the main teratogenic agents for cattle (6,8), and in Brazil, a country well known by its diversity of toxic plants for animals, most important plants causing congenital malformation are *Mimosa tenuiflora* and *Cenostigma pyramidale* (7). Well known plants toxin´s causing congenital malformation in animals are steroidal, quinolizidine, piperidine, or indolizidine alkaloids (5) which are thought to cause reduced fetal movements in the uterus and, consequently, the development of skeletal malformations (2).

Chemical agents, such as medications and chemical products, can also cause anomalies. The most significant ones are those that induce anomalies when used at therapeutic doses, for example, some medications like chloramphenicol, tetracyclines, valproic acid, barbiturates, tranquilizers, and pesticides (8).

Pregnant females, when exposed to environmental or teratogenic agents, can give birth to offsprings with congenital defects, whether the origin is infectious, such as certain viruses (bovine viral diarrhea virus, bluetongue virus, Hog cholera virus, Akabane virus and others) or nutritional, such as nutrient and vitamins deficiency (iodine, copper, manganese, cobalt and vitamin D and A) (9).

Diprosopia has been reported in cats, deer, goats, sheep, rats, cattle and sheep. However, it occurs more frequently in cattle than in sheep and pigs and is rare in goats. Its occurrence is extremely rare in horses (9). Incomplete diprosopia most often has a better prognosis, as it generally presents normal or unaffected internal organs, unlike complete diprosopia, where internal organs duplication always occurs (6,9,10).

References

1. Carles D, Weichhold W, Alberti EM, Léger F, Pigeau F, Horovitz J. Diprosopia revisited in light of the recognized role of neural crest cells in facial development. J Cran Genet Dev Bio 1995;15: 90-97.
2. Gardner DR, Panter KE, Stegelmeier BL, James LF, Ralphs MH, Pfister JA, Schoch TK. Livestock poisoning by teratogenic and hepatotoxic range plants. In: Garland T. & Barr A.C. (Eds), Toxic Plants and Other Natural Toxicants. CAB International, New York 1998: 303-306.
3. Hiraga T, Dennis SM. Congenital duplication. Vet Clin North Am Food Anim Pract 1993;9: 145-61.
4. Hu D, Helms JA. The role of sonic Hedgehog in normal and abnormal craniofacial morphogenesis. Devel 1999;126: 4873-4884.
5. Panter KE, James LF, Gardner DR, Molyneux RJ. The effects of poisonous plants on embryonic and fetal development in livestock. In: Colegate S.M. & Dorling P.R. (ed.). Plant Associated Toxins. Wallingford, CAB International 1994; 325-332.

6. Pavarini SP, Sonne L, Antoniassi NAB, Santos AS, Pescador CA, Corbellini LG, Driemeier D. Anomalias congênitas em fetos bovinos abortados no Sul do Brasil. Pesq Vet Bras 2008; 28: 149–154.
7. Mendonça FS, Riet-Correa F. Plantas que afetam o sistema reprodutor. In: Riet Correa F, Schild AL, Lemos R, Borges JR, Mendonça FS, Machado M. Doenças de ruminantes e equideos. 4. ed. São Paulo: MedVet Editora 2023; 244-247.
8. Rojas M, Walker L. Malformaciones Congénitas: Aspectos Generales y Genéticos. Int J Morphol 2012; 30: 1256–1255.
9. Schild AL. Defeitos congênitos. In: Riet-Correa, F, Schild AL, Lemos RAA, Borges JRJ. Doenças de Ruminantes e Equídeos. 3ª Ed. Santa Maria, Pallotti, 2007: 25-55.
10. Schulze U, Kuiper H, Doeleke R, Ulrich R, Gerdwilker A, Distl O. Familial occurrence of diprosopus in German Holstein calves. Berl Munch Tierarztl Wochenschr 2006;119: 251-257.

*The Diagnostic Exercises are an initiative of the Latin Comparative Pathology Group (LCPG), the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (https://davisthompsonfoundation.org/diagnostic-exercise/).

Associate Editor for this Diagnostic Exercise: Saulo Pavarini
Editor-in-chief: Claudio Barros