


CASE REPORT OPEN ACCESS

Ruminant

Ichthyosis Fetalis in a Lacaune Lamb

Arman Shokri¹ | Afshin Raoofi¹  | Sara Shokrpour² ¹Department of Internal Medicine, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran | ²Department of Pathobiology, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran**Correspondence:** Afshin Raoofi (raoofi@ut.ac.ir)**Received:** 9 January 2025 | **Revised:** 17 March 2025 | **Accepted:** 7 April 2025**Funding:** Self-funded.**Keywords:** hyperkeratosis | ichthyosis | Lacaune | lamb

ABSTRACT

Ichthyosis (inherited congenital condition) is a heterogeneous group of skin cornification and keratinization disorders. Ichthyosis can affect animal and human and characterized by an excessive amount of superficial scale on the skin. A male Lacaune lamb was born alive from a primiparous ewe but it was unable to stand and it was in lateral recumbency and died 12 h after birth. Skin abnormalities included all over hyperkeratosis, cracking in some parts of the body like head and neck. In histopathological investigation of the cutaneous lesions, there was moderate-to-severe thickening of the stratum corneum, with a compact and laminated pattern of orthokeratotic hyperkeratosis, whereas no abnormalities were observed in the other layers of the epidermis. Ichthyosis was diagnosed on the basis of clinical and histopathological findings. In conclusion, ichthyosis in lambs can occur in different forms, but further studies and investigations are needed to accurate classification of this condition in lamb.

1 | Introduction

The skin, the largest organ in the body, has many vital functions, including protection against external physical, chemical and biological assailants, prevention of excessive water loss and regulation of body temperature (Kolarsick et al. 2011). The skin is composed of three layers: the epidermis, dermis and subcutis. The epidermis consists of five layers: the stratum basale (basal), stratum spinosum (spinous), stratum granulosum (granular), stratum lucidum and stratum corneum (cornified). In all forms of ichthyosis, the stratum corneum is the primary site of abnormality (DiGiovanna and Robinson-Bostom 2003). Keratinocytes produced in the basal layer migrate towards the skin surface, undergoing phenotypic changes and differentiation (Gutiérrez-Cerrajero et al. 2023). These phenotypic changes lead to the reorganization of the keratinocyte cytoskeleton, the secretion of lipids into the extracellular space, the formation of intercellular junctions and the terminal differentiation of keratinocytes into corneocytes (Oji et al. 2010; Gutiérrez-

Cerrajero et al. 2023). Any defect in this differentiation process can lead to ichthyosis (Oji et al. 2010; Gutiérrez-Cerrajero et al. 2023).

Ichthyosis, an inherited congenital condition, is a heterogeneous group of disorders affecting skin cornification and keratinization. It can affect both animals and humans and is characterized by an excessive accumulation of superficial scales on the skin, resembling fish scales, with varying degrees of thickening and desquamation (Gutiérrez-Cerrajero et al. 2023; Molteni et al. 2006). In veterinary medicine, the term 'ichthyosis' is used to describe rare congenital or hereditary disorders believed to result from primary defects in the formation of the stratum corneum (Mauldin 2013). However, in humans, this condition can be either acquired or inherited (Gutiérrez-Cerrajero et al. 2023). Inherited ichthyoses are associated with mutations in specific genes encoding proteins involved in the synthesis or metabolism of proteins or lipids essential for keratinocyte terminal differentiation (Gutiérrez-Cerrajero et al. 2023).

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2025 The Author(s). *Veterinary Medicine and Science* published by John Wiley & Sons Ltd.



FIGURE 1 | The lamb in lateral recumbency with hyperkeratotic skin all over the body.

Ichthyosis is a rare condition in sheep, and to our knowledge, there is only one reported case of ichthyosis in a lamb. Many aspects of this condition in lambs remain unknown. Therefore, this report was conducted to describe congenital inherited ichthyosis in a lamb.

2 | Case Report

During the lambing season on a large sheep farm with approximately 10,000 Lacaune sheep, a male lamb was born with an abnormal skin condition. The sheep on this farm were housed in enclosed pens year-round and were fed a balanced total mixed ration (TMR) diet. The lamb was born alive to a primiparous ewe without dystocia. The dam was in good body condition, completely healthy, and had not been treated for any disease during pregnancy.

The lamb was unable to stand and remained in lateral recumbency. As it was unable to suckle, colostrum was administered via a stomach tube.

A physical examination was performed. The heart rate was 120 beats per minute, the respiratory rate was 45 breaths per minute, and the rectal temperature was 39.3°C. Ectropion was evident in both eyes.

Macroscopically, the skin was thickened due to hyperkeratosis. Erythema was observed on the snout (Figure 1). The lamb died 12 h after birth.

There were no obvious gross abnormalities other than skin abnormalities. The skin abnormalities included generalized hyperkeratosis, cracking in certain areas such as the head and neck, ectropion and redness of the snout. Hair was present but trapped within the hyperkeratotic scales.

A necropsy was performed. For histological examination, cutaneous samples (skin from the head and abdominal region) and samples from other organs (liver, spleen and brain) were collected, fixed in 10% neutral buffered formalin, processed, dehydrated, embedded in paraffin wax and sectioned at a thickness of 5 µm using a rotary microtome (RM2 145; Leica, Wetzlar, Germany). The sections were stained with haematoxylin and

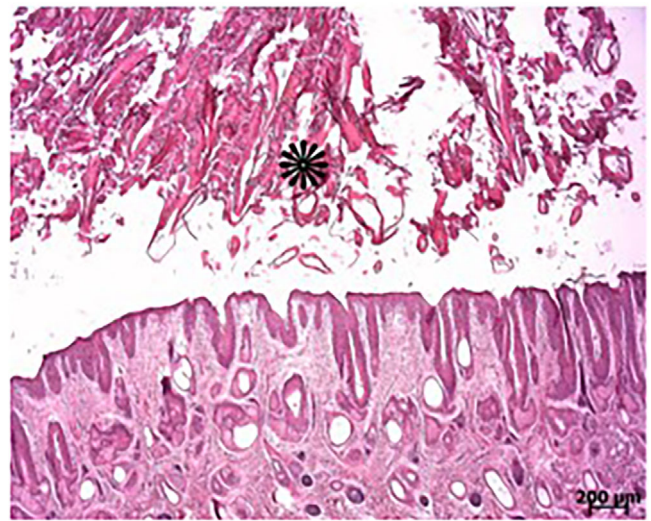


FIGURE 2 | Histopathological findings of nonepidermolytic ichthyosis. Note the orthokeratotic hyperkeratosis (*) contained compact, severely thickened and laminated stratum corneum. H&E, haematoxylin and eosin.

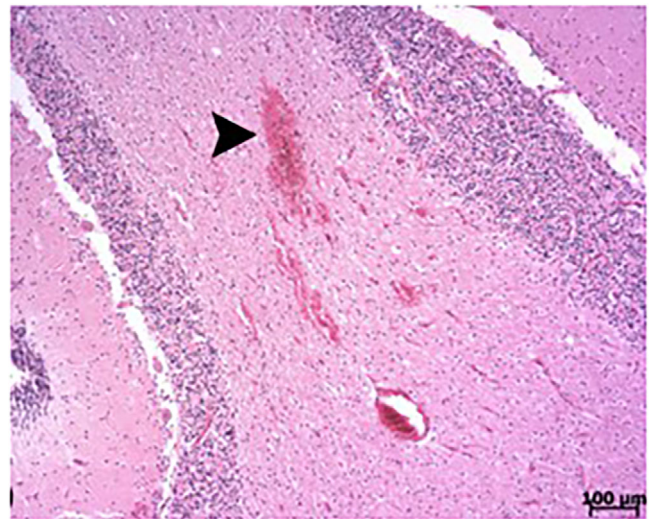


FIGURE 3 | Histopathological findings of cerebellum. Multifocal haemorrhages (arrowheads) in white matter of cerebellum. H&E, haematoxylin and eosin.

eosin, analysed under a light microscope (E600; Nikon, Tokyo, Japan), and representative images were captured.

In histopathological investigation of the cutaneous lesions, there were moderate-to-severe thickening of the stratum corneum, with a compact and laminated pattern of orthokeratotic hyperkeratosis, whereas no abnormalities were observed in the other layers of the epidermis. Plates of the stratum corneum were separated from each other and lifted off the surface. In some sections, hyperkeratosis extended into the follicular infundibulum. On the basis of the macroscopic and microscopic findings, ichthyosis was diagnosed (Figure 2). Additionally, small multifocal haemorrhages were observed in the white matter of the cerebellum (Figure 3).

3 | Discussion

Ichthyosis has been reported in calves (Molteni et al. 2006; Raoofi et al. 2001; Azimpour et al. 2016; Testoni et al. 2006; Cornillie et al. 2007; Cho et al. 2007; O'Rourke et al. 2017; Häfliger et al. 2022), dogs (Mauldin 2013; Mauldin and Elias 2021; Malinová and Čonková 2021; Guaguere et al. 2009), camelids (Taylor 2018), humans (Gutiérrez-Cerrajero et al. 2023; DiGiovanna and Robinson-Bostom 2003) and goats (Edginton et al. 2014). A study has reported ichthyosis in a lamb, and in this study, because of the poor prognosis, the lamb was humanely euthanized at 3 months of age (Câmara et al. 2017). However, the lamb in our study died within a few hours after birth.

The main histopathological features of ichthyosis include severe diffuse orthokeratotic hyperkeratosis with multiple follicular keratosis, mild acanthosis, alopecia with numerous small-sized hairless follicles, or follicles with a significantly reduced hair diameter (Azimpour et al. 2016). In a previous report on ichthyosis in a lamb, histopathological findings included orthokeratotic hyperkeratosis, follicular keratosis with follicular plugging, moderate irregular epidermal hyperplasia and hydropic degeneration. Similarly, hyperkeratosis and epidermal hyperplasia were also observed in our study.

In calves, ichthyosis has been classified into two forms based on severity: ichthyosis fetalis and ichthyosis congenita. Ichthyosis congenita is a milder form, primarily affecting the limbs, abdomen and muzzle, whereas ichthyosis fetalis is a severe form in which affected calves are stillborn or die within hours or days after birth (Raoofi et al. 2001). Ichthyosis in lambs has not yet been classified; however, based on the classification used in cattle, the condition observed in our studied lamb closely resembled ichthyosis fetalis in calves.

In humans, ichthyosis is classified as either non-syndromic (affecting only the skin) or syndromic (affecting both the skin and other organs) (Gutiérrez-Cerrajero et al. 2023). Non-syndromic ichthyoses are further categorized into common ichthyoses (ichthyosis vulgaris and X-linked recessive ichthyosis), autosomal recessive congenital ichthyosis and keratinopathic ichthyoses (Gutiérrez-Cerrajero et al. 2023). Common ichthyoses occur more frequently than other forms and tend to be milder; despite being congenital, desquamation in these patients often develops weeks to months after birth (Gutiérrez-Cerrajero et al. 2023; Traupe et al. 2014). Autosomal recessive congenital ichthyosis is divided into three major clinical phenotypes, with harlequin ichthyosis being the most severe and occasionally fatal form (Takeichi and Akiyama 2016). The lesions observed in our studied lamb closely resembled those of harlequin ichthyosis in humans. However, the classification of ichthyosis requires ultrastructural analysis of skin samples and molecular genetic testing.

The small multifocal haemorrhages observed in the white matter of the cerebellum cannot be definitively attributed to ichthyosis, as this type of haemorrhage is also known to occur in premature fetuses (Limperopoulos et al. 2025). However, as the studied lamb had a normal gestational age, further research is needed to determine whether this lesion is associated with ichthyosis in lambs.

Infectious meningitis and encephalitis can induce white matter haemorrhage (DeBiasi and Tyler 2006; Piquet and Lyons 2016; Jan 2012). However, the absence of inflammation in the histopathology of the white matter of the cerebellum reduces the likelihood of an infectious cause.

In Gaucher disease in lambs, both brain involvement and ichthyosis have been documented (Karageorgos et al. 2011). In this disease, the cerebellar white matter exhibits vacuolation, swollen axons and eosinophilic spheroids in multiple nerve tracts (Karageorgos et al. 2011). Furthermore, small clusters of pale macrophages are occasionally present in the liver's portal areas, and Kupffer cells are frequently distended with fibrillary material, forming characteristic Gaucher cells (Karageorgos et al. 2011). However, none of these histopathological findings were observed in our study. The liver appeared normal, and the only brain abnormality was multifocal haemorrhages in the cerebellar white matter.

Traumatic brain injury can cause white matter haemorrhage (Finnie and Blumbergs 2002). Head trauma may occur during lambing if the ewe stands up quickly, causing the lamb to fall. However, the lambing process was not observed in our study. In general, determining the etiological cause of white matter haemorrhage requires haematological and biochemical analysis, blood gas analysis, toxicology and other diagnostic methods. In our study, we did not follow up on the detection of the etiological cause of white matter haemorrhage, as this finding was only identified during histopathological examination after the lamb's death, and at that time, we did not have access to any samples.

Author Contributions

Arman Shokri: investigation, writing—original draft. **Afshin Raoofi:** supervision, methodology, writing—review and editing. **Sara Shokrpour:** investigation, writing—review and editing.

Acknowledgements

The authors wish to thank everyone who contributed their time and experience to this study.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Peer Review

The peer review history for this article is available at <https://publons.com/publon/10.1002/vms3.70364>.

References

Azimpour, S., F. Sasani, P. Mottaghian, and A. Anoushepour. 2016. "Ichthyosis Congenita in a Calf: Case Report." *Thai Journal of Veterinary Medicine* 46: 517–521.

- Câmara, A. C. L., P. A. C. Borges, S. A. Paiva, F. Pierezan, and B. Soto-Blanco. 2017. "Ichthyosis Fetalis in a Cross-Bred Lamb." *Veterinary Dermatology* 28: 516–525.
- Cho, J.-K., J.-M. Son, D.-S. Lee, S.-J. Park, S.-W. Cho, and S. T. Shin. 2007. "Harlequin Ichthyosis in a HanWoo Calf." *Journal of Veterinary Medical Science* 69: 553–555.
- Cornillie, P., S. Cools, L. Vandaele, and P. Simoens. 2007. "Ichthyosis in the Belgian White and Red Cattle Breed." *Vlaams Diergeneeskundig Tijdschrift* 76, no. 5: 345–351.
- DeBiasi, R. L., and K. L. Tyler. 2006. "Viral Meningitis and Encephalitis." *Continuum: Lifelong Learning in Neurology* 12: 58–94.
- DiGiovanna, J. J., and L. Robinson-Bostom. 2003. "Ichthyosis: Etiology, Diagnosis, and Management." *American Journal of Clinical Dermatology* 4: 81–95.
- Edginton, H. D., D. W. Scott, and E. Olsen. 2014. "Ichthyosis in a Nigerian Dwarf Goat." *Japanese Journal of Veterinary Dermatology* 20: 147–151.
- Finnie, J., and P. Blumbergs. 2002. "Traumatic Brain Injury." *Veterinary Pathology* 39: 679–689.
- Guaguere, E., E. Bensignor, S. Küry, et al. 2009. "Clinical, Histopathological and Genetic Data of Ichthyosis in the Golden Retriever: A Prospective Study." *Journal of Small Animal Practice* 50: 227–235.
- Gutiérrez-Cerrajero, C., E. Sprecher, A. S. Paller, et al. 2023. "Ichthyosis." *Nature Reviews Disease Primers* 9: 2. <https://doi.org/10.1038/s41572-022-00412-3>.
- Häfliger, I. M., C. T. Koch, A. Michel, et al. 2022. "DSP Missense Variant in a Scottish Highland Calf With Congenital Ichthyosis, Alopecia, Acantholysis of the Tongue and Corneal Defects." *BMC Veterinary Research* 18: 20.
- Jan, M. M. 2012. "Meningitis and Encephalitis in Infants and Children." *Saudi Medical Journal* 33: 11–16.
- Karageorgos, L., M. J. Lancaster, J. S. Nimmo, and J. J. Hopwood. 2011. "Gaucher Disease in Sheep." *Journal of Inherited Metabolic Disease* 34: 209–215. <https://doi.org/10.1007/s10545-010-9230-3>.
- Kolarsick, P. A., M. A. Kolarsick, and C. Goodwin. 2011. "Anatomy and Physiology of the Skin." *Journal of the Dermatology Nurses' Association* 3: 203–213.
- Limperopoulos, C., A. J. du Plessis, and J. J. Volpe. 2025. *Cerebellar Hemorrhage. Volpe's Neurology of the Newborn*. Elsevier.
- Malinová, Z., and E. Čonková. 2021. "Ichthyosis in Dogs—Congenital Dermatologic Disorder." *Folia Veterinaria* 65: 22–29.
- Mauldin, E. A. 2013. "Canine Ichthyosis and Related Disorders of Cornification in Small Animals. The Veterinary Clinics of North America." *Small Animal Practice* 43: 89–97.
- Mauldin, E. A., and P. M. Elias. 2021. "Ichthyosis and Hereditary Cornification Disorders in Dogs." *Veterinary Dermatology* 32: e567–e574.
- Molteni, L., S. Dardano, P. Parma, et al. 2006. "Ichthyosis in Chianina Cattle." *Veterinary Record* 158: 412–414.
- O'Rourke, B. A., J. Kelly, Z. B. Spiers, et al. 2017. "Ichthyosis Fetalis in Polled Hereford and Shorthorn Calves." *Journal of Veterinary Diagnostic Investigation* 29: 874–876.
- Oji, V., G. Tadini, M. Akiyama, et al. 2010. "Revised Nomenclature and Classification of Inherited Ichthyoses: Results of the First Ichthyosis Consensus Conference in Sorèze 2009." *Journal of the American Academy of Dermatology* 63: 607–641.
- Piquet, A. L., and J. L. Lyons. 2016. "Infectious Meningitis and Encephalitis." In *Seminars in Neurology*, 367–372. Thieme Medical Publishers.
- Raoofi, A., S. Mardjanmehr, and S. Nekoei. 2001. "Ichthyosis Congenita in a Calf in Iran." *Veterinary Record* 149: 563.
- Takeichi, T., and M. Akiyama. 2016. "Inherited Ichthyosis: Non-Syndromic Forms." *Journal of Dermatology* 43: 242–251.
- Taylor, S. D. 2018. *Hyperkeratotic Skin Conditions in New World Camelids*. Società Nazionale Alpaca e Lama.
- Testoni, S., V. Zappulli, and A. Gentile. 2006. "Ichthyosis in Two Chianina Calves." *Deutsche Tierärztliche Wochenschrift* 113: 351–354.
- Traupe, H., J. Fischer, and V. Oji. 2014. "Nonsyndromic Types of Ichthyoses—An Update." *JDDG: Journal Der Deutschen Dermatologischen Gesellschaft* 12: 109–121.