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CLINICAL CASES REPORTS

Metastatic squamous cell carcinoma with suspected *Mycobacterium tuberculosis* complex infection in an adult male llama (*Lama glama*)

*Carcinoma escamocelular metastásico con sospecha de infección por el complejo
Mycobacterium tuberculosis en una llama macho adulta (Lama glama)*

*Carcinoma de células escamosas metastático com suspeita de infecção pelo complexo
Mycobacterium tuberculosis em uma lhama macho adulta (Lama glama)*

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Abstract

Introduction: Squamous cell carcinoma (SCC) is a malignant epithelial neoplasm that occurs infrequently in South American camelids but has significant metastatic potential. **Anamnesis:** A 16-year-old male *Lama glama* presented with lethargy, sternal recumbency, and anorexia. Clinical findings included a laceration on the left carpus, abdominal and axillary edema, bilateral inguinal lymphadenomegaly, and generalized weakness. Supportive treatment with fluid therapy, broad-spectrum antibiotics, and anti-inflammatory drugs was initiated without clinical improvement. Due to progressive deterioration, the animal was euthanized, and a complete necropsy was performed. **Clinical and laboratory findings:** The initial differential diagnosis included infections caused by *Mycobacterium* spp. Examination revealed erosions of the left metacarpal joint, subdermal abscesses, ventral subcutaneous edema, hemothorax, and multiple white nodules on the parietal pleura. Microscopically, cutaneous lesions showed a malignant epithelial neoplasm with concentric keratin, necrosis, abnormal mitoses, and megakaryocytes. Lesions in the lungs, diaphragm, and intercostal muscles were identified as metastases. **Results:** The definitive diagnosis was metastatic squamous cell carcinoma. **Conclusion:** The findings demonstrate that epithelial neoplasms should be considered within the differential diagnosis of chronic or granulomatous cutaneous lesions in camelids, even when clinical signs suggest an infectious etiology.

Keywords: *histopathology; immunohistochemistry; Lama glama; metastases; oncology; pathogenesis; skin; tumor.*

Resumen:

Introducción: El carcinoma de células escamosas (CCE) es una neoplasia maligna epitelial de presentación poco frecuente en camélidos sudamericanos, pero con potencial metastásico significativo. **Anamnesis:** Llama macho de 16 años presenta letargia, decúbito esternal y anorexia. Los hallazgos clínicos incluyen laceración en el carpo izquierdo, edema abdominal y axilar, linfadenomegalia inguinal bilateral y debilidad. Se instauró tratamiento de soporte con fluidoterapia, antibióticos de amplio espectro y antiinflamatorios, sin mejoría clínica. Debido

al deterioro progresivo, el animal fue eutanasiado y se realizó necropsia completa. **Hallazgos clínicos y de laboratorio:** El diagnóstico diferencial inicial contempló infecciones por *Mycobacterium* spp. El examen reveló erosiones en la articulación metacarpiana izquierda, abscesos subdérmicos, edema subcutáneo en zonas ventrales, hemotórax y nodulaciones blancas en la pleura parietal. Microscópicamente, las lesiones cutáneas mostraban neoplasia maligna de células epiteliales, queratina concéntrica, necrosis, mitosis anormales y megacariocitos. Las lesiones en pulmones, diafragma y músculos intercostales se identificaron como metástasis. **Resultados:** El diagnóstico definitivo fue carcinoma escamoso metastásico. **Conclusión:** Los hallazgos evidencian que las neoplasias epiteliales deben considerarse dentro del diagnóstico diferencial de lesiones cutáneas crónicas o granulomatosas en camélidos, incluso cuando las manifestaciones clínicas sugieren una etiología infecciosa.

Palabras clave: *histopatología; inmunohistoquímica; Lama glama; metástasis; oncología; patogénesis; piel; tumor.*

Resumo:

Introdução: O carcinoma de células escamosas (CCE) é uma neoplasia epitelial maligna de ocorrência rara em camelídeos sul-americanos, mas com potencial metastático significativo. **Anamnese:** Um macho de *Lama glama* com 16 anos apresentou letargia, decúbito esternal e anorexia. Os achados clínicos incluíram laceração no carpo esquerdo, edema abdominal e axilar, linfadenomegalia inguinal bilateral e fraqueza generalizada. Instituiu-se tratamento de suporte com fluidoterapia, antibióticos de amplo espectro e anti-inflamatórios, sem melhora clínica. Devido ao agravamento progressivo, o animal foi submetido à eutanásia e realizada necropsia completa. **Achados clínicos e laboratoriais:** O diagnóstico diferencial inicial considerou infecções por *Mycobacterium* spp. O exame revelou erosões na articulação metacarpiana esquerda, abscessos subdérmicos, edema subcutâneo ventral, hemotórax e múltiplos nódulos esbranquiçados na pleura parietal. Microscopicamente, as lesões cutâneas apresentaram neoplasia epitelial maligna com queratina concêntrica, necrose, mitoses anormais e megacariócitos. As lesões nos pulmões, diafragma e músculos intercostais foram identificadas como metástases. **Resultados:** O diagnóstico definitivo foi de carcinoma de células escamosas metastático. **Conclusão:** Os achados demonstram que as neoplasias epiteliais devem ser consideradas no diagnóstico diferencial de lesões cutâneas crônicas ou granulomatosas em camelídeos, mesmo quando os sinais clínicos sugerem uma etiologia infecciosa.

Palavras-chave: *histopatologia; imuno-histoquímica; Lama glama; metástases; oncologia; patogênese; pele; tumor.*

Introduction

Squamous cell carcinoma (SCC) in llamas is a clinically relevant entity among skin neoplasms in New World camelids. A retrospective study has shown that SCC is one of the most frequently diagnosed tumors in these species, especially in older animals (Aboellail et al., 2021). The most common sites of occurrence are the gastric compartments, skin, mammary glands, and third eyelid; in addition, metastasis may develop in regional lymph nodes or distant sites (Aboellail et al., 2021).

Granulomatous lesions in llamas can arise from a range of etiological agents, including *Mycobacterium* complex (Jankovsky and Donnell., 2018). In particular, mycobacterial infections such as those caused by *Mycobacterium microti* have been reported to produce multiple caseous nodules and necrosis with acid-fast bacilli, representing critical differential diagnoses for cutaneous masses in this species (Oevermann et al., 2004). Since camelids are often in close contact with humans through activities such as hiking or petting zoos, they represent a potential source of zoonotic infections. In this context, it is essential to consider the *Mycobacterium tuberculosis* complex in the differential diagnosis, given its ability to cause debilitating diseases characterized by granulomatous lesions and respiratory signs (Oevermann et al., 2004).

Within veterinary oncology, it has been emphasized that the use of special stains and immunohistochemistry (IHC) is essential to improve diagnostic accuracy when histomorphological mimics complicate the recognition of squamous cell carcinoma (SCC). Markers such as p40, p63, or CK5/6 are particularly valuable for confirming squamous differentiation and excluding other epithelial etiologies (Alomari et al., 2014; Ramos-Vara et al., 2002). In this context, the present report describes a case of metastatic SCC in a llama, carefully considering infectious differential diagnoses to illustrate the diagnostic challenges encountered in camelid pathology.

The present case reports a 16-year-old male llama (*Lama glama*) that exhibited progressive weakness, edema, lymphadenomegaly, and hypoproteinemia, with a presumptive clinical

diagnosis of chronic hepatic disease and severe parasitism; during necropsy, infection with the *Mycobacterium tuberculosis* complex and metastatic SCC were suspected.

Case presentation

A 16-year-old male llama (*Lama glama*), weighing 150 kg, is reported with a history of lethargy, sternal recumbency, and anorexia. Upon clinical examination, a body condition score of 2.5/5 was noted, along with respiratory signs, a laceration on the left forelimb carpus, ventral and axillary abdominal edema, bilateral inguinal lymphadenomegaly, weakness, and persistent sternal recumbency. The animal's diet included concentrate, kikuyu grass, and silage, with a deworming protocol every 2-3 months using fenbendazole or albendazole in rotation.

A complete blood count and blood chemistry revealed mild anemia, hypoproteinemia, and hypoalbuminemia. The initial clinical diagnosis was chronic hepatic fibrosis and severe gastrointestinal parasitism. The animal was treated with furosemide, betamethasone, and oxytetracycline. Due to the progression of the animal's clinical condition, euthanasia was performed, followed by necropsy at the National University of Colombia.

Macroscopically, the necropsy revealed subcutaneous edema in the ventral regions. The skin exhibited multiple erosions and ulcers on the left metacarpal joint and the left costal wall, as well as several subdermal abscesses in the axillary region and along the midline. Opening the thoracic and abdominal cavities revealed hemothorax, with abundant yellowish fluid in the pericardium and adhesions to the epicardium. Multiple white nodulations were seen on the parietal pleura, extending to the visceral surface of the intercostal muscles, diaphragm, and lungs. These nodules protruded from the parenchyma with a gritty, white appearance upon sectioning. Similar nodules were found in the liver, kidneys, and spleen (Figure 1), findings that raised suspicion of infection by the *Mycobacterium tuberculosis* complex. In the gastrointestinal tract, the mucosa exhibited extensive areas of congestion, particularly in the third gastric compartment, along with approximately 0.5 cm-sized white nodulations. Tissue samples were collected for microscopic examination, microbiological studies, and molecular biology analyses.



Figure 1. Cutaneous lesions and nodulations in *Lama glama*. A) Dermal lesion with erosion and ulceration at the forearm-metacarpal joint (MAI) (arrows). B) White, friable nodulations (arrows) adhered to the diaphragm, measuring 0.5 * 0.5 cm. C) A 2 * 2 cm nodule with gritty content located in the left lung. D) White, friable nodulations (arrows) adhered to the visceral surface of the intercostal muscles.

Microscopically, the skin lesions were identified as malignant neoplastic lesions, with epithelial cells forming islands, trabeculae, and cords within the superficial and deep dermis. These lesions were accompanied by foci of concentric laminar keratinization and necrosis. The cells exhibited moderate atypia, with severe anisocytosis, anisokaryosis, and nuclear pleomorphism, including the presence of megakaryocytes (greater than 20 microns). More than 30 mitotic figures were counted in 10 HPF in a 2.37 mm² area, many of which were atypical. The nodular lesions found in the pulmonary parenchyma, diaphragm, adipose tissue, and intercostal muscles were identified as metastatic foci of the tumor. Also, marked multifocal infiltrates composed of lymphocytes, some plasma cells, macrophages, and neutrophils were observed, with multifocal moderate hemorrhage (Figure 2).

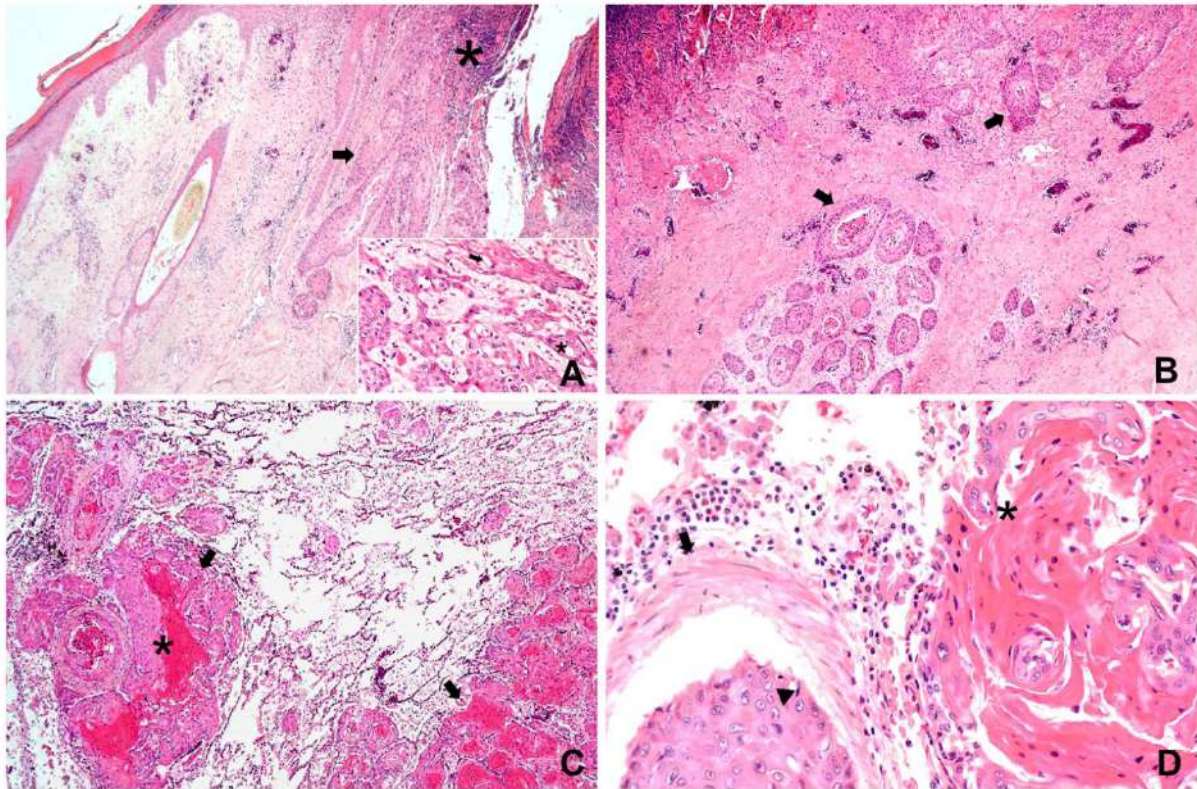


Figure 2. Squamous cell carcinoma in *Lama glama*. A) H&E, skin: Squamous cell carcinoma infiltrating the superficial and deep dermis, arranged in trabeculae and cell nests (arrow). Epidermal ulceration with associated inflammatory process is observed (*). Inset: the tumor is organized in trabeculae (arrow), showing marked cellular and nuclear pleomorphism, pronounced anisokaryosis and anisocytosis, and atypical mitotic figures (*). B) H&E, skin: Squamous cell carcinoma infiltrating the deep dermis. Nests of neoplastic cells surrounded by desmoplastic stroma. (arrows). C) H&E, lung: Multiple metastatic foci of malignant epithelial neoplastic proliferation (arrows), and keratin pearls (*). D) H&E, lung: Cellular and nuclear pleomorphism is observed, with an adjacent secondary inflammatory process. The neoplasm invades the alveoli, arranged in nests or trabeculae with central keratinization, forming keratin pearls (*) and vascular invasion (arrowhead) characterized by neoplastic cells withing the lumen of blood vessels (arrow).

Immunohistochemistry was performed on the analyzed tissues, revealing strong immunolabeling for cytokeratin (CK) and expression of p63 immunolabeling (Figure 3). Microbiological and molecular analyses (PCR) of necropsy samples were negative for the *Mycobacterium tuberculosis* complex and other agents that could cause lesions similar to those observed at necropsy. Based on the gross and microscopic lesions, together with molecular

testing and immunohistochemistry, a metastatic squamous cell carcinoma was determined as the final diagnosis.

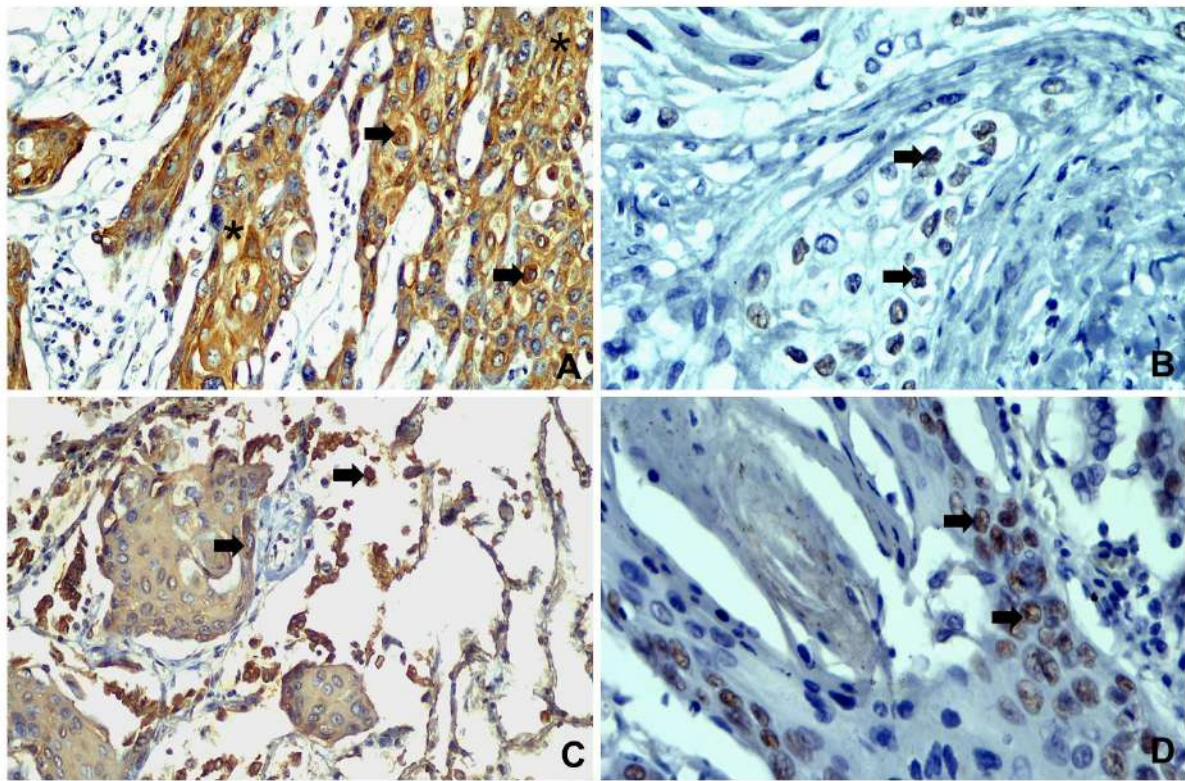


Figure 3. Immunohistochemical expression of cytokeratin (CK) and p63 in squamous cell carcinoma in *Lama glama*. A) (CK). Immunohistochemistry of skin shows intense immunoreactivity in the neoplastic epithelial proliferation (arrow), with an invasive, non-circumscribed pattern, arranged in nests (*). B and D) (p63). Immunohistochemistry of skin and lung demonstrating multifocal nuclear immunolabelling in neoplastic cells (arrow). C) (CK). Immunohistochemistry lung showing strong immunoreactivity in metastatic epithelial proliferation (arrow).

Discussion

This report describes the first case of squamous cell carcinoma in *Lama glama* in Colombia and, to the authors' knowledge, one of the few reports of metastasis to tissues such as the lungs in this species. It is recommended that both neoplastic and non-neoplastic lesions be considered as differential diagnoses for cutaneous mass-forming lesions, with particular emphasis on histopathological differentiation.

Neoplasms in New World camelids are rare; however, several types have been documented over the past 25 years, including gastric squamous cell carcinomas, multicentric lymphosarcoma, gemistocytic astrocytoma, uterine adenocarcinoma, and cutaneous squamous cell carcinoma in the sternal region (Rogers et al., 1997; Aboellail et al., 2021). Among the most common neoplasms in cutaneous and mucocutaneous areas are fibropapillomas, squamous cell carcinomas, and fibrosarcomas. Squamous cell carcinomas typically affect the hairy skin, perineal tissue, and ocular regions and are the most common malignant neoplasm in llamas (Valentine and Martin, 2007).

Squamous cell carcinomas associated with wounds have been documented, with the carcinoma appearing 20 to 40 years after the initial injury. In some cases, the original wound does not heal, with neoplastic tissue developing between 3 and 12 months later. In this case, although the animal had ulcerated and eroded lesions, no prior trauma or wounds were reported that could be associated with "wound-associated cancers" (Rogers et al., 1997). Nonetheless, this should be considered a differential diagnosis for traumatic lesions that fail to improve with treatment. Neoplasms in scar tissue have been reported in other species, including mast cell tumors and squamous cell carcinomas in dogs, fibrosarcomas and squamous cell carcinomas in horses with chronic wounds, and horn core cancer in *Bos indicus* linked to chronic trauma from horn trimming (Baird and Frelief, 1990; Fressler et al., 1993).

A study by Kretsch et al., reported a 19-year-old male llama with regional and distant metastatic oral squamous cell carcinoma, presenting with severe respiratory distress, submandibular edema, and bicavitary effusion. The llama in this case had respiratory signs, ventral abdominal and axillary edema, and bilateral inguinal lymphadenomegaly, findings similar to those described by Rogers et al., in a 12-year-old female llama with cutaneous squamous cell carcinoma in the sternal region. The presence of swollen, adherent, and firm inguinal lymph nodes in this case suggests that regional or distant metastasis should be suspected when edema, respiratory signs, and lymphadenomegaly are present. Differential diagnoses in such cases include chronic drainage tracts associated with foreign bodies, vertebral abscesses, sequels, aberrant parasitic larval migration, and infections by *Mycobacterium tuberculosis* complex (Rogers et al., 1997).

The animal presented multiple white nodules in the thoracic cavity, on the parietal pleura, intercostal muscles, diaphragm, and lungs, which protruded from the parenchyma and had a gritty, white appearance upon sectioning. Similar lesions were noted in the liver, kidneys, and

spleen. Pulmonary nodules with a cinnamon or brown color and viscous centers, typically seen in squamous cell carcinoma metastasis, were not observed in this case (Hollis, 2024; Kretsch et al., 2022; Taulescu et al., 2012). These findings are not pathognomonic for squamous cell carcinoma metastasis, as similar appearances have been noted in other pulmonary neoplasms. Clinical signs observed in this patient, such as progressive weight loss, anorexia, lethargy, dyspnea, pleural effusion, and pericardial effusion, are similar to those seen in patients with pulmonary adenosquamous carcinomas and cholangiocarcinoma (Ramos-Vara et al., 2002; Taulescu et al., 2012).

Histologically, the skin lesions showed epithelial cells forming islands, trabeculae, and cords in the superficial dermis, with concentric keratin foci, necrosis, and pleomorphism. These findings were consistent with those reported by Rogers et al., where invasive circular groups of cells with central keratin pearls were observed. However, mitotic figures were considerably lower in their case, likely due to earlier histopathological diagnosis.

In the lungs, multiple neoplastic foci with features similar to those of the skin lesions were observed, resembling bronchoalveolar carcinomas (Moser et al., 2019). These lesions are typically characterized by abundant, poorly cellular neoplastic acinar structures, plump spindle cells, and extracellular collagen deposition. Occasionally, areas of squamous epithelial differentiation, with central keratin pearls and without apparent acinar formation, can be observed. This contrasts with pulmonary adenoplastic carcinomas, in which the acini are lined by cuboidal to columnar epithelium, sometimes with cilia (Ramos-Vara et al., 2004; Ramos-Vara et al., 2002). Furthermore, SCC are typically neoplasms that secondarily induce extensive inflammatory and necrotic processes (Kretsch et al., 2022; Rogers et al., 1997). In the present case, necrosis and inflammation resulting from neoplastic activity were associated with the development of hemothorax and the macroscopically evident exudate.

It has been reported that pulmonary metastatic lesions in thoracic radiographs of llamas are characterized by a diffuse pattern of thousands of nodules, while in alpacas, the radiographic findings show unstructured interstitial patterns, findings similar to those observed in mammary carcinoma metastases in dogs. Despite the lack of specific radiographic studies for the detection of metastases in New World camelids, it is important to consider those animals that present radiographic patterns such as those mentioned (Gall et al., 2006).

The presence of p63 and CK expression is a strong indicator of squamous differentiation, supporting the identification of squamous cell carcinomas and their distinction from other spindle-cell or mesenchymal tumors. In this case, the immunohistochemical profile was particularly relevant, as the granulomatous foci could have been mistaken for *Mycobacterium tuberculosis* complex. A strong immunolabeling for cytokeratin (CK) and the expression of p63 in this case are findings similar to those reported in other species, such as camels, alpacas, dogs, and humans with squamous cell carcinomas (Rosiers et al., 2020; Mestrinho et al., 2014; Chandratre et al., 2017; Cardoso et al., 2025). These results highlight the usefulness of immunohistochemistry, as molecular biomarkers produced by neoplastic cells provide valuable information about the biological status of the tumor and can be applied to assess disease progression and the effectiveness of therapeutic interventions (Cardoso et al., 2025).

Cisplatin and doxorubicin are commonly used to treat squamous cell carcinoma in llamas, although treatment for metastatic disease is often ineffective at therapeutic doses, leading to potential toxicity. Piroxicam has shown effectiveness in treating oral squamous cell carcinoma in dogs and horses, making it a possible therapeutic alternative for cases with local metastasis in llamas (Moore et al., 2003).

In this study, a Ziehl–Neelsen stain for the detection of *Mycobacterium* spp. was not performed, as the histopathological findings did not suggest the presence of acid-fast bacteria and the analysis was therefore considered unnecessary. This is acknowledged as a limitation; nonetheless, the use of molecular assays to exclude *Mycobacterium* infection provides reliable support for the diagnostic interpretation.

Conclusions

This case represents one of the first reports of pulmonary metastasis in a llama due to squamous cell carcinoma, highlighting the possibility that this neoplasm can spread to organs such as the lungs, liver, kidneys, and spleen.

Although neoplasms in llamas are rare, it is important to consider both neoplastic and non-neoplastic lesions when diagnosing cutaneous masses. Additionally, proper histopathological differentiation is essential to avoid misdiagnoses, as various types of neoplasms can affect these animals, including squamous cell carcinoma and fibropapillomas.

For the treatment of squamous cell carcinomas, treatments such as cisplatin and doxorubicin are mentioned, although their effectiveness in metastatic diseases is limited and can have toxic effects. The use of piroxicam is also suggested as a therapeutic alternative for certain cases, based on previous studies in other species such as dogs and horses.

The immunohistochemistry and molecular findings support a diagnosis of metastatic squamous cell carcinoma. Nevertheless, given the overlapping features with granulomatous processes, additional diagnostic tools such as immunohistochemistry may further strengthen future reports.

Declarations

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author contributions

TP and LB conceptualized, designed the methodology, supervised, funding acquisition, Project administration, and managed the research. SM and TP writing – original draft, Writing – review & editing.

Use of Artificial Intelligence (AI)

No AI or AI-assisted technologies were used during the preparation of this work.

Data availability

The data sets used in the current study are available from the corresponding author on request.

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