



Fibrosarcoma en ovinos de la zona altiplánica del Perú: reporte de casos

Ovine fibrosarcoma in the plateau high lands of Peru: Case report

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Resumen

Las enfermedades neoplásicas afectan notoriamente la salud de los ovinos y por tanto, la rentabilidad de la crianza de esta especie. Con la finalidad de realizar un estudio macro y microscópico de dos casos de cáncer abdominal, se tomó una borrega (caso 1) procedente del distrito de Umachiri, provincia de Melgar, zona norte del departamento de Puno y otra borrega (caso 2) procedente del distrito de Laraqueri, provincia de Puno, zona sur oeste del mismo departamento; ambas zonas pertenecen al sector peruano de la meseta del Collao. Los dos especímenes se encontraban padeciendo de enfermedad crónica caquectizante sin respuesta a ningún esquema terapéutico. Las dos borregas se recibieron como casos patológicos a estudiarse en el Curso de Patología Veterinaria General de la Facultad de Medicina Veterinaria y Zootecnia (FMVZ) de la Universidad Nacional del Altiplano de Puno (UNAP). Ambos animales fueron sacrificados por eutanasia utilizando pentobarbital sódico. Se hizo la necropsia de ambos casos en el Laboratorio de Patología macroscópica de la FMVZ, UNAP, se tomaron muestras para el estudio microscópico; las muestras se procesaron en el Laboratorio de Histopatología de la mencionada facultad. Los resultados fueron los siguientes: macroscópicamente, en la cavidad abdominal del caso 1, se observó numerosos nódulos blanquecinos de diferentes tamaños, bordes irregulares, firmes al tacto e invadiendo tejidos adyacentes incluyendo ganglios linfáticos mesentéricos; en el mesenterio del caso 2, se observó un solo nódulo blanquecino de consistencia firme, con bordes muy irregulares, invadiendo algunas asas intestinales cercanas; microscópicamente, en ambos casos se observó tejido fibroso anaplásico, conformado por fibroblastos pleomórficos, atípicos y algunos se observaron multinucleados; en el caso 1, además, se constataron numerosos focos necróticos en proceso de calcificación. Estos hallazgos macroscópicos de lesiones nodulares pálidas, de forma irregular, firmes al tacto y resistentes al corte; que al examinarlas microscópicamente se observó tejido fibroso pobremente diferenciado, en estos dos casos estudiados, permiten concluir que corresponden a fibrosarcoma, siendo el caso 1, de carácter terminal.

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Abstract

Neoplastic diseases affect notoriously the health of the sheep and therefore, the profitability of the breeding of this species. In order to perform a macro and microscopic study of two cases of abdominal cancer, a sheep was taken (case 1) from the district of Umachiri, province of Melgar, north zone of the department of Puno, and another sheep (case 2) from the district of Laraqueri, province of Puno, southwest area of the same department; both zones belong to the Peruvian sector of the Collao plateau high lands. The two specimens were suffering from chronic weakening disease without response to any therapeutic scheme. The two ewes were received as pathological cases to be studied in the Course of General Veterinary Pathology of the Faculty of Veterinary Medicine and Zootechnics (FMVZ) of the National University of Altiplano in Puno city (UNAP). Both animals were sacrificed by euthanasia using sodium pentobarbital. Necropsy was performed in both cases in the FMVZ's Laboratory of Macroscopic Pathology of UNAP, tumor tissue samples were taken for the microscopic study; The samples were processed in the Histopathology Laboratory of the aforementioned faculty. The results were as follows: macroscopically, in the abdominal cavity of case 1, numerous whitish nodules were observed, with irregular edges, firm to the touch invading adjacent tissues including numerous mesenteric lymph nodes; in the

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mesentery of case 2, a single whitish nodule of firm consistency was observed, with very irregular borders and quite invasive to adjacent intestinal loops; microscopically, in both cases, anaplastic fibrous tissue was observed, conformed by pleomorphic fibroblasts, some multinucleated and atypical; in case 1, in addition, numerous necrotic tumor tissue in process of calcification foci were found. These macroscopic findings of nodular-pale lesions, irregularly shaped, firm to the touch, and resistant to cut; that when examined microscopically, poorly differentiated fibrous tissue was observed, in these two cases studied, allow us to conclude that they correspond to fibrosarcoma and the case 1 was a terminal one.

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Introduction

Sheep is a cosmopolitan animal that mainly produces meat and wool, whose breeding in Peru is a competitive and profitable activity¹ even though its population has been declining from 23 million in 1961 to 9.5 million by 2012². Puno region owning 26% of the national population of sheep is the first producer of ovine in Peru³.

Various ailments cause the deterioration of these animals' health, for example, tumor diseases such as ovine pulmonary carcinoma (OPC), a disease not only highly prevalent in the country, but also highly contagious and deadly, causes great economic losses in the sheep industry^{4,5}. Other types of cancer such as squamous cell carcinoma affect this species as well⁶.

Cancer of fibrous tissue, known as fibrosarcoma, according to the World Health Organization (WHO) is a highly malignant tumor disease of mesenchymal origin in which other types of histological structures such as bone and cartilage are absent⁷. Fibrosarcoma consists of a pathological proliferation of fibroblasts⁸, frequently affects dogs and cats, infrequently to equines, bovines, and pigs and rarely to other species⁹. This type of malignant neoplasm derives from connective tissue, it is characterized by fibrous tissue anaplasia¹⁰, it has no predilection for any sex but frequently to adults and it can develop anywhere

on the animal's body⁹. This type of neoplasm can be circumscribed or infiltrative, have a whitish or graish coloration, can be soft or firm to palpation, is generally resistant to cutting, and lacks a connective tissue capsule¹¹. Histologically, fibrosarcoma is characterized by the of presence an interlocking network of collagen fibers^{12,13}, some other components of connective tissue, and cancerous fibroblasts. Varying degrees of differentiation can be found in this type of neoplastic tissue, in some cases of this type of cancer that are classified as differentiated fibrosarcomas, elongated spindle-shaped fibroblasts arranged in interlocking fascicles, hyperchromatic nuclei cells but cell atypia or many mitotic figures are observed¹². Other cases of this type of cancer which are categorized as the intermediate or moderately differentiated degree of malignancy present certain cellular atypia. In the cases that are considered as poorly differentiated fibrosarcomas exist evident fibroblast mitotic activity, cellular atypia, and a notable connective stroma^{14,15}.

The etiology of fibrosarcoma has been related to several carcinogenic substances, subcutaneous administration of vaccines, microchip implants, chronic inflammations¹⁸, ionizing radiation, cytostatics¹⁶, and genetic disorders related to p53 or RB113 gene mutation in mammals or sarcoma retrovirus infections in chickens¹⁷.

In the aforementioned context, the objective of this report was the macroscopic and microscopic characterization of fibrosarcoma in ovine from the plateau highland area of the department of Puno in Peru.

Description of clinical cases

Animals and Clinical History. For the report, two cases of fibrosarcoma were taken in sheep from two areas of the Peruvian highlands.

Case 1. A 4-year-old Corriedale breed sheep from the Chuquibambilla Research and Production Center (CRPC) of the National University of Altiplano-Puno (UNAP), located in Umachiri district, Melgar province, in the northern area of Puno department. The animal suffered from a very chronic disease, anorexia and had a very poor physical condition, did not respond to any therapeutic scheme, at the end it fell into prostration and was sacrificed

Case 2. A 5-year-old half-blood sheep from a peasant community in Laraqueri district, Puno province, in the southwest area of Puno department. It suffered from a chronic illness, had poor physical conditions, and did not respond to any treatment.

The anamnesis and clinical examination of both animals revealed that they were suffering from chronic and weakening disease and they were received as pathological cases to be studied in the General Veterinary Pathology course of the Faculty of Veterinary Medicine and Zootechnics (FVMZ) of the National University of Altiplano in Puno city (UNAP).

Sampling

Both specimens were sacrificed using sodium pentobarbital and the necropsy technique was performed

in order to characterize and interpret the macroscopic findings. The lesions were examined and samples of the tumor tissues and regional mesenteric lymph nodes were taken for histopathological study.

Pathological Study

In order to interpret the macroscopic characteristics of the tumor lesions in both cases and to identify possible metastases in regional lymph nodes, macroscopic pathological study of both specimens was carried out at the Laboratory of Macroscopic Pathology of the FVMZ, UNAP. Samples were taken from both the tumor tissue and the regional lymph nodes, fixing them in 12% formalin, they were embedded in paraffin, 5 µm sections were made and staining with hematoxylin-eosin were made. The microscopic characteristics were interpreted in the Histopathology Laboratory of FVMZ, UNAP.

Macroscopic Pathology

Case 1. The specimen was in a very cachectic state, went into prostration, and was sacrificed. Examination of the abdominal cavity organs revealed the presence of numerous nodules ranging in size from barely visible to approximately 5cm in diameter in all organs of this cavity (figure 1). These nodules had irregular edges, pale coloration, without capsule, firm consistency, and quite resistant to cutting. Some of these nodules were very firm in consistency with a certain stony appearance and exaggerated cut resistance. Numerous mesenteric lymph nodes were found to be enlarged, firm in consistency, resistant to cut, and with an appearance similar to the nodules present in other abdominal organs.

Figure 1 Case 1, macroscopic image of the liver, note numerous pale to grayish nodules



Figure 2 Case 2, macroscopic image of the section of a pale nodule invading adjacent tissue



Case 2. The specimen was quite cachectic. The macroscopic examination revealed the presence of a nodule with extremely irregular edges, pale in color, firm consistency, resistant to cutting and conspicuously invading some adjacent tissues such as the mesentery and some intestinal loops (figure 2) causing reduction of the lumen of the affected segments. A mesenteric lymph node near this node was found to be very swollen, pale in color, resistant to cutting,

with a similar appearance to the original node, and surrounded by a jelly-like substance (figure 3).

Figure 3 Case 2, macroscopic image of lymphadenomegaly in the mesenteric lymph node



Histopathology

Case 1. Microscopically, in the examined nodules it was observed very disordered fibrous tissue, notably polymorphic cells, elongated or oval fibroblasts, and some of them with hyperchromatic nuclei. Some mitotic figures of fibroblasts, as well as some of these multinucleated cells (figure 4) and a large amount of extracellular matrix components, were noted. Another histopathological characteristic of this case was the presence of necrosis foci of the tumor tissue with an amorphous and bluish hue appearance due to the calcification process (Figure 5). In the sampled lymph nodes, infiltration of fibrosarcomatous tumor tissue with characteristics similar to those found in the main tumor nodules surrounded by a relatively normal appearance lymphoid tissue was observed; some areas of necrosis in process of dystrophic calcification were noted as well.

Figure 4 Case 1. Microscopic image of fibrosarcoma, note fibroblasts with hyperchromatic, elongated or oval nuclei and some multinucleated fibroblasts (H-E, 40x)

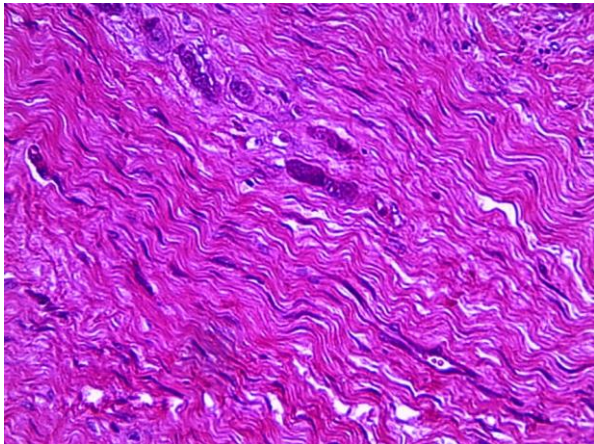
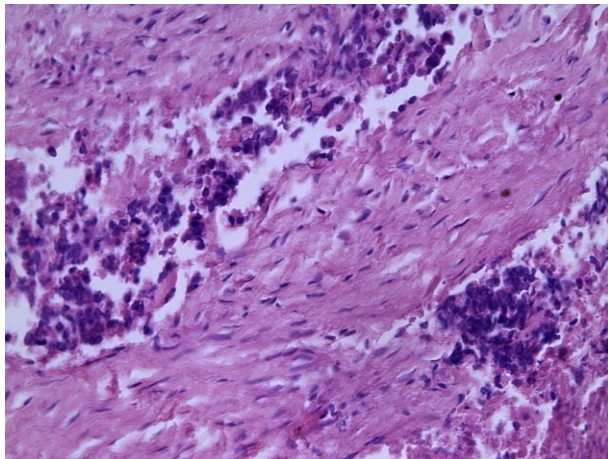
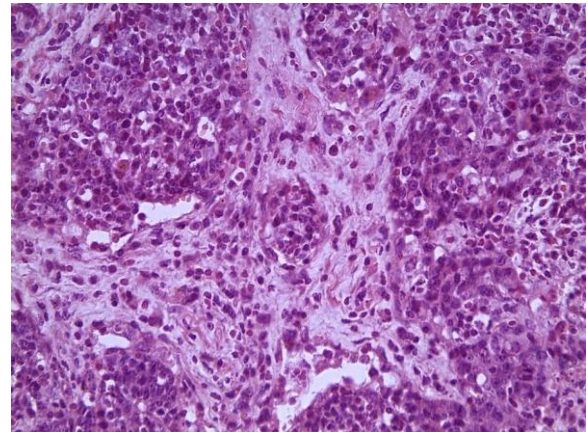


Figure 5 Case 1. Microscopic image of fibrosarcoma, note areas of necrosis in the process of calcification surrounded by anaplastic fibroblasts (H-E, 40x)



Case 2. A disorderly arrangement of notoriously pleomorphic fibroblasts surrounded by thick bundles of connective tissue fibers was observed. Multinucleated and/or hyperchromatic fibroblasts were also evident. In the regional lymph node sampled, anaplastic fibrous tissue with characteristics similar to those found into the in situ tumor nodule, surrounded by a relatively distorted lymphoid tissue was observed (figure 6).

Figure 6 Case 2. Microscopic image of metastatic fibrosarcoma in the mesenteric ganglion, note the neoplastic micronodules surrounded by lymphoid tissue (H - E, 40x)



Discussion

Macroscopic Pathology

The two cases of cancer of fibrous tissue in sheep from the highland area of Peru, subject of this report, case 1 with multiple metastases to various organs and regional lymph nodes and case 2 with a single original nodule and metastases in one mesenteric lymph node, were observed in the abdominal cavity. In various domestic species, connective tissue cancers can be located in different segments of the body, for example, in Colombia, Vallejo Timarán et al.⁹ reported a dermal fibrosarcoma on the mandibular border of a bovine, while Valentine & Martin¹⁸ reported tumors of this type located on the lips, gums, maxilla, and cornea in alpacas and llamas; some other cases of this malignant tumor may be located in deep soft tissues or near the bones¹⁰, in the genital organs such as the vulva or vagina²³ or in any other part of the body^{8,9,16,20}.

The macroscopic morphology of the two cases of connective tissue sarcomas in sheep, presenting ir-

regular borders, an irregular surface, and the lack of fibrous capsule, are characteristic of this type of tumor^{23,24}. In both studied cases the neoplasms infiltrative ones into the adjacent tissues and particularly case 1 was very invasive and this morphological peculiarity corresponds to fibrosarcomas²¹. The tonality of the connective tissue cancer is usually whitish to greyish^{8,18,21} and the consistency is generally firm^{9,16}, these macroscopic characteristics were also observed in the specimens studied. However, in case 1, the nodules were found to be quite firm in consistency and when cutting them, strong resistance and a certain crackling sound, and a certain stony appearance were noted.

The metastatic capacity of any cancer, such as fibrosarcoma, is characteristic^{23,21}, although some cases of this type of cancer do not necessarily cause metastasis⁸, but the cases of the present report did and especially the case 1 in which numerous metastatic nodules were observed in various organs including the lymph nodes of the abdominal cavity.

Histopathology

The histopathological appearance of poorly differentiated fibrous tissue made up of fibroblasts that adopt very elongated shapes in some cases and oval ones in other cases, surrounded by an extracellular matrix of thick fiber bundles, as observed in both reported cases, are characteristic of malignant connective tissue tumors^{24,23}. The presence of fibroblasts containing more than one nucleus and/or more intensely colored or hyperchromatic are characteristic of fibrous tissue cancers^{23,25,26}, as well as the presence of some mitotic figures are observed in this type of tumors^{14,27} and are peculiarities that were observed in these two cases. However, in the case 1,

the reason for this report, the presence of numerous necrotic foci, in some of the nodules, with an amorphous histopathological appearance adopting various bluish tones, denoting an evident dystrophic calcification process were noted. This type of Necrotic lesions in malignant tumors is generally caused by hypoxia and/or anoxia due to angiogenesis deficiency in the neoplastic mass^{28,29,30}.

In the Peruvian highlands, this is the first report of fibrous tissue cancer in sheep, and as such it constitutes a contribution to veterinary oncology. Different types of cancers occur in this area, such as the highly prevalent and of retroviral etiology ovine pulmonary carcinoma (OPC)⁵, and squamous cell carcinoma⁶, whose etiology of which is most likely ionizing radiation. Establishing with certainty the etiology of these two cases of fibrosarcoma is complicated, however, as risk factors for this type of pathologies, some genetic, infectious, and environmental factors have been considered¹⁶, and as determining factors, the mutations caused by ionizing radiation and certain chemical carcinogens^{16,17}.

The pathological characteristics of these nodules, which are whitish to greyish in color, with a firm consistency, a certain stony appearance as in case 1, with notoriously irregular edges and quite infiltrating adjacent tissue and accompanied by lymphadenopathy in the abdominal cavity of both ewes; neoplasms in which, upon microscopic observation, a clearly anaplastic tissue made up of pleomorphic and atypical fibroblasts containing hyperchromatic nuclei or some of them being multinucleated and bundles of disorderly arranged fibers of connective tissue in the interstitial areas, were indicators that allowed us to conclude that these two cases correspond to fibrosarcoma.

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The authors of this work have not received any type of funding for the development of the research, neither the authorship nor the publication of this article, so no conflict of interest is generated.

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Ethical aspects

During the execution of this investigation case report, no faults were incurred. In the intervention we have taken into account human sensitivity without realizing discomfort, anguish and pain of the animals, for this we took the use of the appropriate anesthesia and analgesia protocol.

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