

Giant Cell-rich Extraskelatal Osteosarcoma in the Maxillary Region of a Saanen Goat: A Case Report

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Abstract

A 9-year-old female Saanen goat died following swelling of the right cheek and loss of appetite. Necropsy revealed a subcutaneous mass on the right cheek measuring 7 × 5 × 5 cm and another mass on the dorsal soft palate measuring 5 × 5 × 5 cm. Neither mass was continuous with the maxillary bone. Histopathological examination showed that both masses were predominantly composed of atypical spindle-shaped cells. Osteoclast-like multinucleated giant cells were frequently observed, along with scattered osteoid formation and calcified osteoid tissue. Immunohistochemical analysis revealed that the tumor cells were positive for vimentin but negative for keratin. Based on these findings, the mass was diagnosed as a giant cell-rich extraskelatal osteosarcoma, representing only the first such case reported in a goat.

Discipline: Animal Science

Additional key words: subcutaneous cheek tissue, immunohistochemistry, osteoid formation

Introduction

Osteosarcoma is a malignant mesenchymal tumor characterized by the formation of osteoid by tumor cells. It is classified into skeletal osteosarcoma, which arises in association with the bone, and extraskelatal osteosarcoma, which occurs in soft tissues unrelated to the bone—with the majority being skeletal osteosarcomas (Chung & Enzinger 1987). Osteosarcomas predominantly affect the limb bones of dogs and cats, accounting for up to 85% of malignant bone tumors in dogs and approximately 70% in cats (Thompson et al. 2015). Although cases have been reported in other domestic animals such as cattle, horses, and sheep (Bush et al. 2007, Nagamine et al. 2014, Thompson et al. 2015), osteosarcoma is extremely rare in goats. To date, only three cases involving the humerus, mandible, and thoracic cavity have been documented (Braun et al. 2011, Domenis et al. 2018, Steinberg &

George 1989).

In this report, we present a case of extraskelatal osteosarcoma occurring in the subcutaneous tissue of the cheek region in a Saanen goat.

Material and methods

1. Animal

A 9-year-old female Saanen goat, kept on a farm with three companion animals in Fukui Prefecture, Japan, died unexpectedly. Lameness in the right forelimb was noted on 13 April 2024 and initially improved following hoof trimming and disinfection. However, the attending veterinarian observed swelling in the right cheek area and advised continued monitoring. On 7 May, during a follow-up examination prompted by the animal expelling feed that had been chewed, the swelling had increased in size. A 4 cm mass and unchewed roughage

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lodged in the oral cavity were observed. Symptomatic treatment with antibiotics was initiated, but the goat's appetite declined, and its overall condition gradually deteriorated. The animal died on the night of 20 May. The goat was submitted to Fukui Prefectural Livestock Hygiene Service Center for a pathological examination to identify the cause of death.

2. Histological and immunohistochemical examination

During necropsy, tissue samples were collected from the liver, spleen, kidneys, heart, lungs, stomach, small intestine, colon, tongue, trachea, brain, and masses in the cheek and oral cavity. The samples were fixed in 10% neutral-buffered formalin and embedded in paraffin for histological examination. Paraffin-embedded sections were prepared and stained with hematoxylin and eosin (HE) following standard protocols. Serial sections of the masses were additionally stained with Azan staining, Watanabe's silver staining, periodic acid-Schiff (PAS) reaction, von Kossa reaction, and phosphotungstic acid-hematoxylin (PTAH) staining. Immunohistochemistry (IHC) was performed using the following primary antibodies: anti-vimentin (mouse monoclonal, clone VIM3B4; PROGEN, Heidelberg, Germany), anti-keratin (mouse monoclonal, clone AE1/AE3; DAKO, Glostrup, Denmark), anti-smooth muscle actin (SMA; mouse polyclonal, DAKO), and anti-desmin (mouse monoclonal, clone D33; Abcam, Tokyo, Japan). A commercial detection kit (Histofine Simple Stain MAX-PO (MULTI), Nichirei Bioscience Inc., Tokyo, Japan) and 3,3'-diaminobenzidine tetrahydrochloride (Histofine Simple Stain DAB solution; Nichirei Bioscience) were used for IHC processing.

3. Bacterial examination

For bacterial analysis, samples from the liver, spleen, kidneys, heart, lungs, cerebrum, and subcutaneous mass in the cheek were cultured on 5% sheep blood agar medium and deoxycholate hydrogen sulfide lactose agar. The cultures were incubated at 37°C for 24 h in a 5% CO₂ atmosphere.

Result

1. Gross findings

Necropsy revealed emaciation and swelling of the right cheek (Fig. 1). A subcutaneous mass in the right cheek measuring 7 × 5 × 5 cm was observed, and a 5 × 5 × 5 cm mass was present on the dorsal soft palate (Fig. 2). Both masses were firm-elastic and solid, with a rough and necrotic surface. Neither mass was continuous with

the maxilla. A detached posterior maxillary molar was embedded in and attached to the soft palate mass. Grossly, the subcutaneous mass had displaced the maxillary posterior molar and extended into the oral cavity through the gap left by the missing tooth, forming a continuous lesion with the soft palate mass. On the cut surface, both masses exhibited milky-white areas with petechial hemorrhages and dark red necrotic regions (Fig. 3). No tumor involvement of the existing bone was noted. The oral mass did not obstruct the oral cavity, and the goat was able to eat. Additional findings included a 0.5 × 1 cm focal necrosis at the center of the tongue, collapse (expansion failure) of the right lung, and accumulation of red, foamy fluid in the trachea. A rope measuring 35 × 1.5 cm, presumed to have been ingested, was also found in the rumen.

2. Histopathological findings

Histological examination of the cheek mass revealed proliferation of spindle-shaped tumor cells arranged in bundles or storiform patterns, extending from the dermis into the subcutaneous tissue (Fig. 4). The tumor cells had oval-to-pleomorphic nuclei with one or more prominent nucleoli and fusiform eosinophilic cytoplasm. The nuclei showed marked size variation and atypia, and mitotic figures were frequently observed. Numerous osteoclast-like multinucleated giant cells (Fig. 4), along with scattered areas of fine osteoid formation, calcified osteoid tissue (Fig. 5), hemorrhage, necrosis, and stromal fibrosis, were observed. Interstitial fibers were stained dark blue by Azan and red with Watanabe's silver stain. Osteoid tissue within the mass stained intensely blue with Azan throughout most of its area (Fig. 6), and a portion was positive for PAS reaction (Fig. 7), whereas the calcified tissue stained positively with von Kossa staining. The superficial layer of the mass showed extensive necrosis, severe hemorrhage, neutrophilic infiltration, and fibrin deposition, which stained blue with PTAH staining. The oral tumor displayed histological features similar to those of the cheek mass. Additional findings included ruminal mucosal erosions and ulcers on the tongue. No metastatic lesions were detected in the other examined organs.

3. IHC

Immunohistochemically, spindle-shaped cells and multinucleated giant cells in the mass were diffusely positive for vimentin (Fig. 8) and negative for keratin (Fig. 9), SMA, and desmin.



Fig. 1. External appearance
Swelling of the right cheek (arrow) with facial deformity is visible.

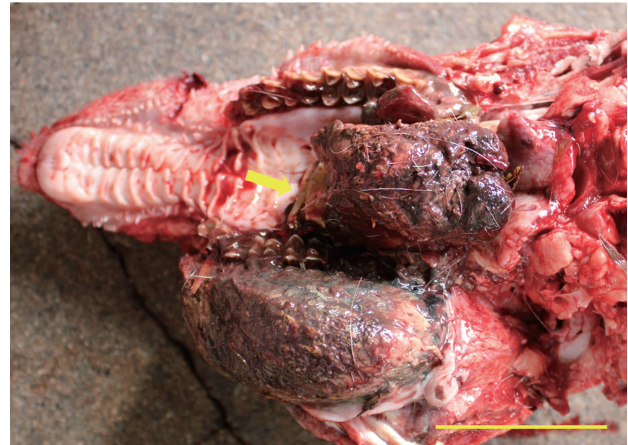


Fig. 2. Necropsy findings of the skull with the mandible removed

An ovoid mass is present in the subcutaneous tissue of the right cheek to the dorsal soft palate. The soft palate mass is attached to the dislodged posterior maxillary molar (arrow). Bar = 5 cm

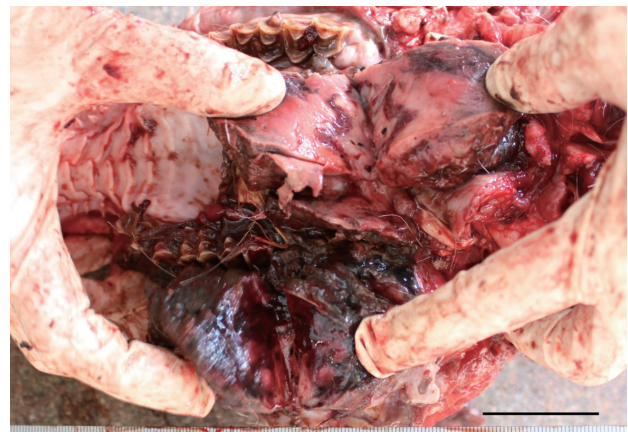


Fig. 3. Necropsy findings of the skull

The surface of the mass appears rough and necrotic. The cut surface shows a mixture of milky-white and dark-red necrotic areas. Bar = 3 cm

4. Bacteriological findings

Bacteriological examination revealed no significant bacterial isolates from the internal organs or cerebrum. However, several opportunistic pathogens—including *Moraxella bovis*, *Pasteurella canis*, and *Acinetobacter lwoffii*—were isolated from the subcutaneous and soft palate mass of the cheek.

Discussion

In this case, ovoid masses were observed in the subcutaneous tissue of the cheek and the dorsal soft

palate. Histologically, the tumor was composed of spindle-shaped cells positive for vimentin, exhibiting marked cellular atypia and numerous mitotic figures, including atypical forms, consistent with a diagnosis of sarcoma. The presence of frequent multinucleated giant cells, along with scattered osteoid formation and calcified osteoid tissue, supported the diagnosis of giant cell-rich extraskelatal osteosarcoma (Dittmer et al. 2022).

In osteosarcoma, tumor cells secrete bone matrix components such as glycogen and collagen fibers into the extracellular space, similar to osteoblasts. The accumulation of these secretions may contribute to the

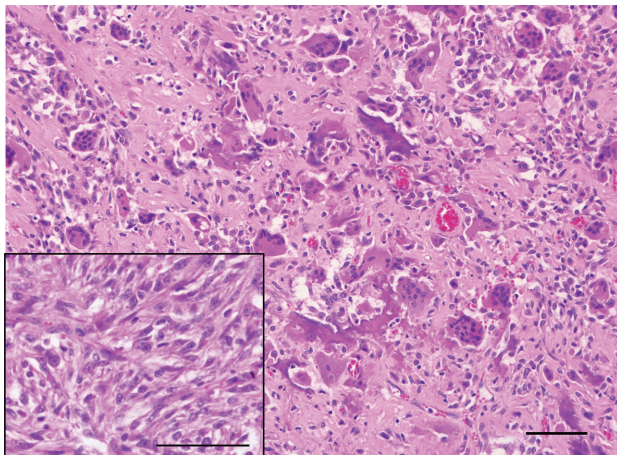


Fig. 4. Histopathological findings of the mass
Proliferation of spindle-shaped bundles or storiform patterns (lower left) and frequent multinucleated giant cells are observed. Bar = 50 μ m

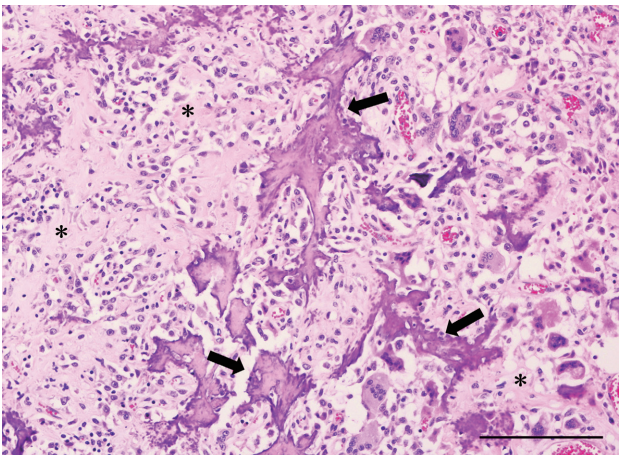


Fig. 5. Histopathological findings of the mass
Scattered osteoid formation (*) and calcified osteoid (arrows) are observed within the tumor. Bar = 100 μ m

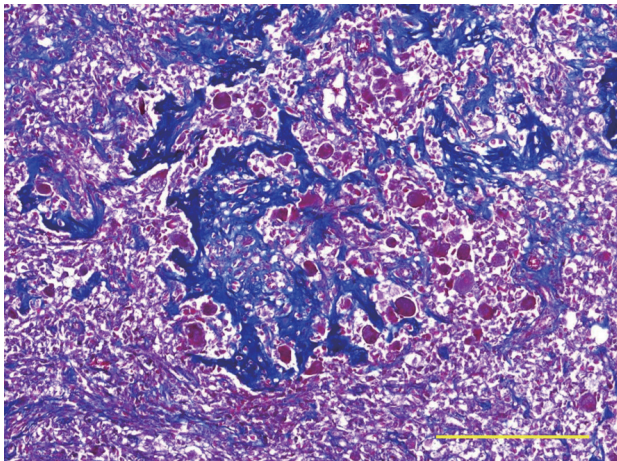


Fig. 6. Histopathological findings of the mass
Osteoid within the mass stained intensely blue with Azan. Bar = 200 μ m

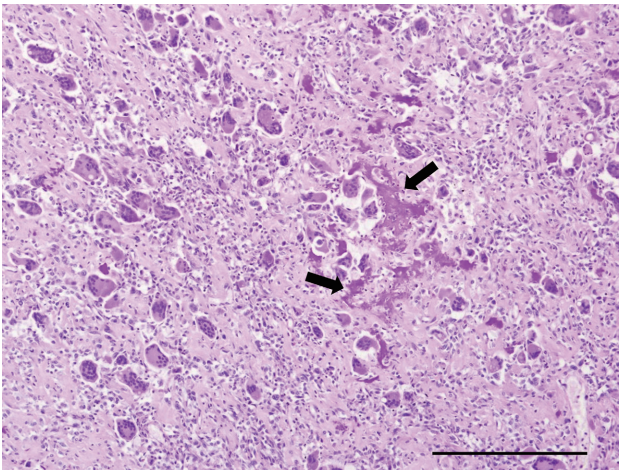


Fig. 7. Histopathological findings of the mass
Osteoid in the mass stained positively (arrows) with the periodic acid-Schiff reaction. Bar = 200 μ m

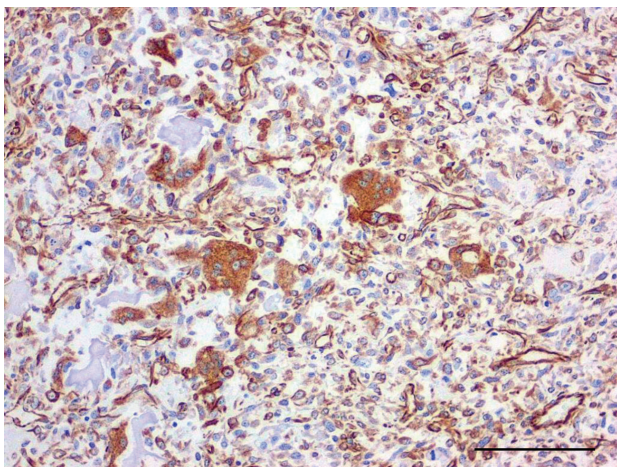


Fig. 8. Immunohistochemical findings of the mass
Spindle-shaped and multinucleated giant cells stain positive for anti-vimentin antibody. Bar = 100 μ m

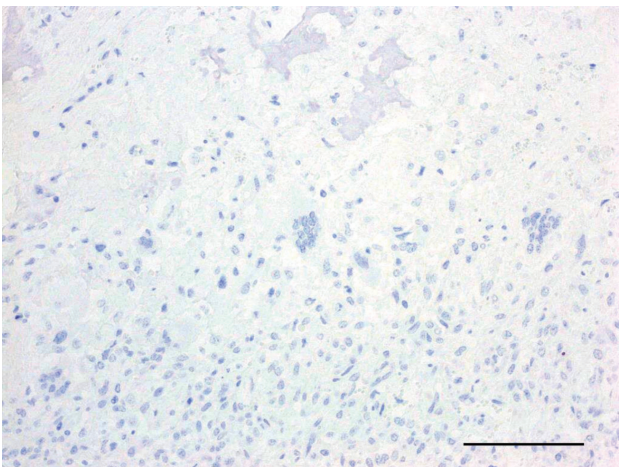


Fig. 9. Immunohistochemical findings of the mass
Spindle-shaped cells and multinucleated giant cells are negative for anti-keratin antibody. Bar = 100 μ m

formation of bone-like hard tissue (Suto et al. 2014). Consistent with previous reports, the osteoid tissue in this case was intensely stained blue with Azan and showed partial positivity with the PAS reaction. Differential diagnoses for osteosarcoma include other sarcomas, extraskelatal osteomas, and heterotopic ossification (Dittmer et al. 2022). Other sarcomas can be distinguished by the absence of neoplastic osteoids (Dittmer et al. 2022). The absence of malignant features, such as pronounced pleomorphisms, can distinguish extraskelatal osteomas from heterotopic ossifications. Differential diagnoses of giant cell-rich extraskelatal osteosarcoma include giant cell tumors of bone, nonossifying fibromas, and other sarcomas such as undifferentiated pleomorphic sarcoma. Giant cell tumors of the bone arise within the bone and can be distinguished by the absence of malignant features such as atypical mitoses and pronounced pleomorphism (Biermann et al. 2024, Dixon et al. 2016). Nonossifying fibromas can be differentiated by the lack of dysplasia and absence of osteoid formation (Murphy et al. 2011). Undifferentiated pleomorphic sarcoma and other sarcomas can be distinguished primarily by the absence of neoplastic osteoid tissue, as previously mentioned (Dittmer et al. 2022, Matsuda et al. 2009). IHC is rarely definitive for diagnosing osteosarcoma, as no marker is currently known to specifically label osteosarcoma tumor cells (Dittmer et al. 2022). Development of functional markers for accurate diagnosis is anticipated in the future.

Extraskelatal osteosarcoma is a rare tumor first reported in humans in 1941 and accounts for approximately 1%-2% of soft tissue sarcomas (Chung & Enzinger 1987, Haga et al. 2011). Unlike skeletal osteosarcoma, which typically affects young individuals, extraskelatal osteosarcoma is more common in adults, particularly those in their 40s to 60s, with an average age at diagnosis of 51 years (Sordillo et al. 1983). As in humans, the incidence of extraskelatal osteosarcoma in dogs is low, accounting for less than 2% of all osteosarcomas (Patnaik 1990). In dogs, extraskelatal osteosarcomas have been reported in various soft tissues, including the duodenum, esophagus, trachea, lungs, heart, skin, subcutaneous tissue, spleen, liver, and kidneys, with occasional metastasis to the lymph nodes, lungs, heart, liver, and stomach (Mochizuki et al. 2009).

In contrast, reports of extraskelatal osteosarcoma in cattle and goats are rare, with only three cases documented: one in the neck of a 5-year-old cow (Braun et al. 2010), one in the abdominal cavity of a 16-year-old cow (Suto et al. 2014), and one in the thoracic cavity of a 16-year-old goat (Braun et al. 2011). Extraskelatal osteosarcoma is considered highly malignant and

associated with a poor prognosis. In dogs, the median and mean survival times are 25 days (Langenbach et al. 1998) and 23 days (Patnaik et al. 1990), respectively—shorter than those for skeletal osteosarcoma (Patnaik et al. 1990). In the present case, the affected goat was 9 years old and died 37 days after the initial diagnosis, a survival period consistent with reports in both humans and dogs.

Consistent with skeletal osteosarcomas, fibroblastic, osteoblastic, chondroblastic, and giant cell-rich (osteoclastic) subtypes have also been reported in extraskelatal osteosarcoma (Bane et al. 1990, Patnaik 1990, Weiss & Goldblum 2001). In cattle, one case each of the chondroblastic and osteoblastic subtypes has been documented (Braun et al. 2010, Suto et al. 2014). Due to frequent observation of osteoclast-like multinucleated giant cells, the present case could be classified as a giant cell-rich (osteoclast-type) extraskelatal osteosarcoma.

Several large-scale studies investigating the prevalence of neoplasia in goats have shown that neoplastic conditions are relatively common (Bildfell et al. 2002, Löhr 2013). However, osteosarcoma is extremely rare in this species. In a review of spontaneous tumors in goats by the Veterinary Diagnostic Laboratory at Oregon State University (Löhr 2013), various tumor types were identified, including lymphomas, cutaneous squamous cell carcinomas, thymomas, mammary adenocarcinomas, and malignant melanomas; however, osteosarcoma was not included.

Differential diagnoses of a mass lesion in the maxillary region should also include bacterial infections. Actinomycosis is one of the primary causes of mass formation in the mandibular and maxillary region in cattle (Mauldin & Peters-Kennedy 2015). In the present case, actinomycosis was ruled out due to the absence of a suppurative granuloma identified on histopathological examination. Although not performed in this case, anaerobic culture testing is useful for differentiating actinomycosis (Valour et al. 2014). No significant bacteria were isolated in the bacterial culture, suggesting that other bacteria, such as facultative anaerobes and microaerophiles, were not involved in the lesion and death in this animal.

The present case was the second case of extraskelatal osteosarcoma reported in a goat and the first to be diagnosed as the giant cell-rich subtype. The clinical progression and histological features observed here were consistent with those reported in humans, dogs, and cattle. Although osteosarcoma is rare in domestic animals, it should be considered in the differential diagnosis when evaluating tumors in goats.

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