Tumori dell'apparato scheletrico degli animali domestici

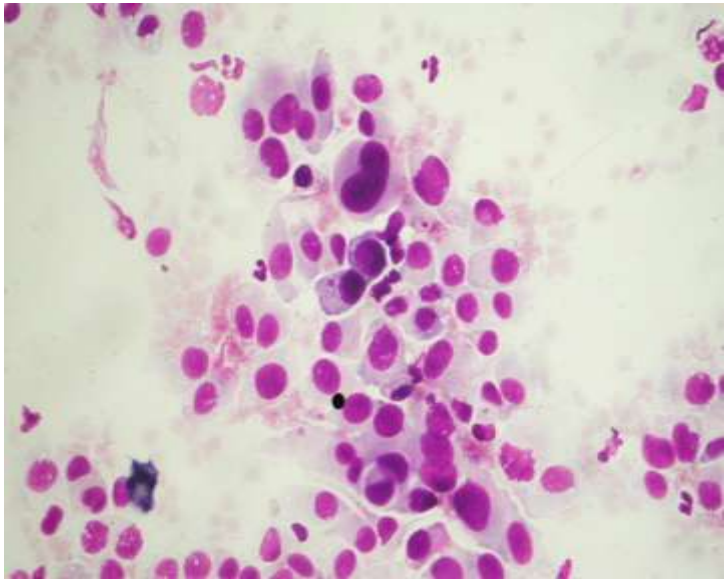
Leonardo Leonardi
UNIVERSITA' DEGLI STUDI DI PERUGIA

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Animali e uomo alleati contro il cancro: attualità e nuove prospettive.
I tumori in medicina comparata: oncogenesi spontanea umana ed animale

Giovedì 21 marzo 2013 – Camera dei Deputati – Palazzo Marini - Roma

(WHO, 1994)



BENIGNI

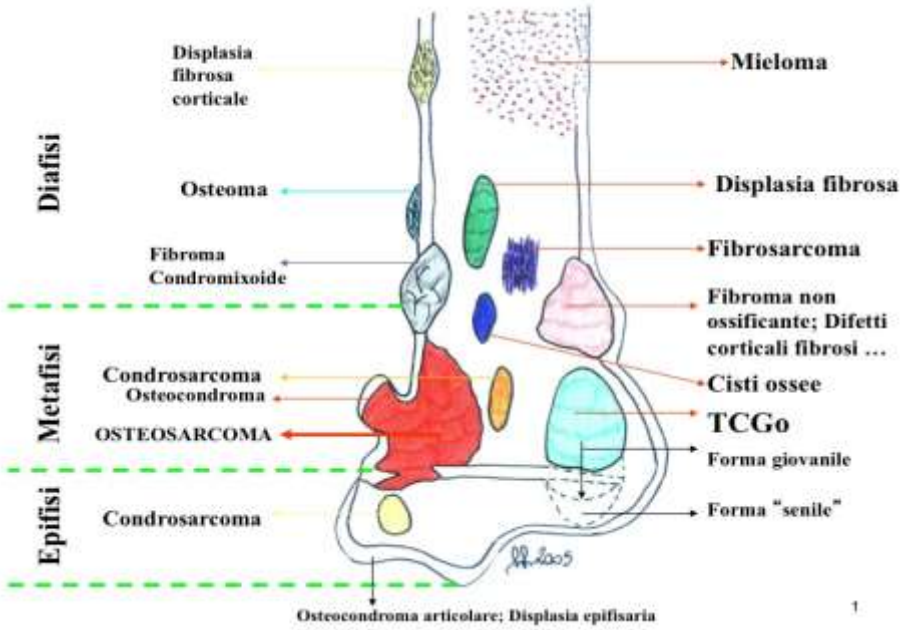
- **OSTEOCONDROMA**

MALIGNI

- **OSTEOSARCOMA;**
- **CONDROSARCOMA.**

ARTICOLARI

- SARCOMA SINOVIALE.



FREQUENZA



> 6,5 PBS/100,00

2% BENIGNI 98% MALIGNI

- ↑ METASTASI POLMONARI
- ↑ OSTEOSARCOMA
- ↑ FIBROSARCOMA
- ↑ EMANGIOSARCOMA
- ↓ OSTEOCONDROMA

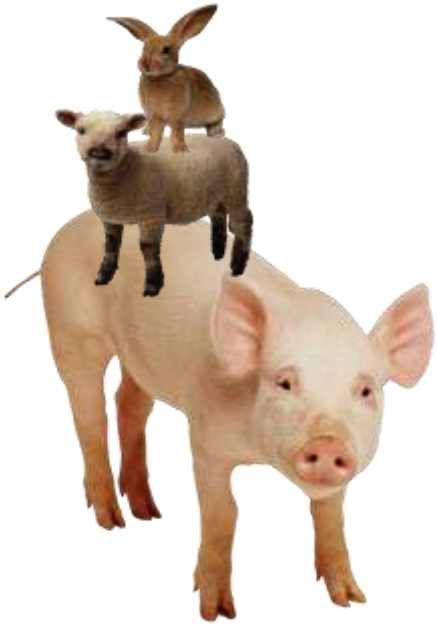


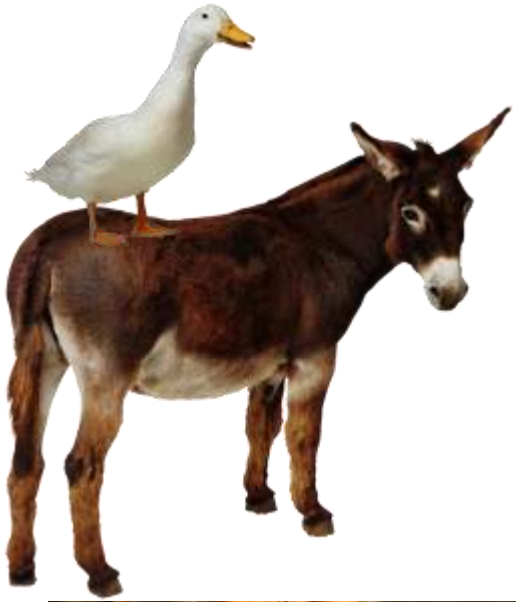
< 3,1 PBS/100,00

BENIGNI Vs MALIGNI

- ↓ METASTASI POLMONARI
- ↑ CONDROSARCOMA
- ↑ FIBROSARCOMA
- ↓ EMANGIOSARCOMA
- ↑ OSTEOCONDROMA

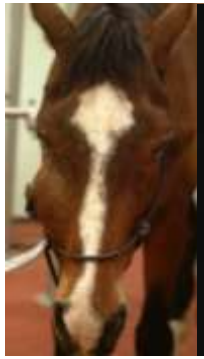
ALTRE SPECIE ANIMALI:

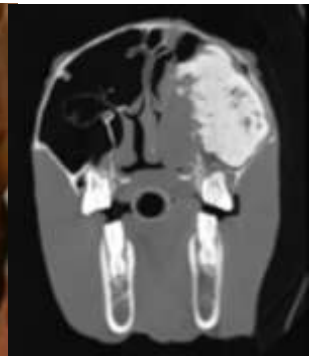


















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Available online at: http://www.bioinfo.in/contents.php?id=70

PARIOSTEAL FIBROUS MAXILLARY OSTEOSARCOMA IN A HORSE: A CASE REPORT

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**Università di Perugia – Dipartimento di Patologia, Diagnostica e Clinica Veterinaria – Via San Costanzo, 4 - 06126 Perugia – Italia
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Abstract: Osteosarcoma is the most frequent malignant bone tumor in domestic animals and humans, representing 80-85% of malignant bone tumors in dogs [3, 15] and about 75-75% in cats. Only a few cases of osteosarcomas have been reported in horses with the majority in the head and neck region [1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16]. Clinical signs are usually associated with a slow growing mass, lameness and interference with mastication [3, 6]. We describe a case of primitive parosteal fibrous maxillary osteosarcoma in a 15 year old English Arabian horse, hospitalized first for a clinical diagnosis of sinusitis. This case is also unusual in that generally maxillary fibrous osteosarcoma in horses are found in the rostral part of the maxilla [1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16] while this one was found in the caudal maxillary sphenoid cavity spread to a regional lymph node but the bone tissue was preserved for examination, confirming that was indeed a case of osteosarcoma.

Key words: parosteal osteosarcoma, horse, maxilla, fibrous osteosarcoma, juxtacortical osteosarcoma

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Text

Osteosarcoma is a malignant neoplasm of bone, in which malignant osteoblasts produce osteoid and immature bone [7]. The most characteristic feature of the osteosarcomas is the production of osteoid [7]. Osteosarcoma is a rare tumor in horses and is usually poorly classifiable, because it has no specific staining reaction. The tumor is highly malignant and usually metastasizes early. Osteosarcomas is the most frequent bone tumor in dogs, representing 80-85% of malignant and it represent 80% of all malignant bone tumors in dogs [5, 13] and 75% in cats [2]. Tumors of the head and neck are very rare in horses [1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16] and only 1% of all cutaneous carcinomas of the head and neck region [17]. The majority of reported cases of equine osteosarcomas occurred in the head and neck region [1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16]. The jaw is the predominant subtype in Scottish-D, osteosarcomas [3]. Many factors have been hypothesized to play a role in pathogenesis of osteosarcomas in humans and animals, including viruses, chemicals, radiation, trauma, foreign bodies, and genetic factors [7]. Chronic bone infarcts, osteomyelitis, arthritis, skeletal diseases and disorders and other host factors such as body size and sex [13]. Pain and swelling are the most frequent clinical signs [3, 6]. Metastasis to the lungs and/or enlargement of the regional lymph nodes [3]. Serological findings are not pathognomonic but increased alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) have been reported as unfavorable prognostic factors [3].

Case report

A 15 year old Anglo-Arabian horse presented to the Veterinary School of the University of Perugia with a large, firm painful mass on the left face.

The horse, had bilateral purulent nasal discharge, normal shape and motility of the nostrils, reduced air flow on the right, and regi-

UN CASO DI OSTEOSARCOMA FIBROBLASTICO OMERALE IN UN LEONE (*PANTHERA LEO*)

Leonardi Leonardo[1], Lepri Elvio[1], Friedrich Klaus[2], Olivieri Oliviero[3], Mechelli Luca[1]

A.I.P.Vet. IX Congresso Nazionale 25-26 maggio 2012 - Perugia

TUMORI OSSEI EXTRASCHELETRICI: OSA

- **Mammella**
- Cute
- Muscolo scheletrico
- Ovaio
- Milza
- Ghiandole surrenali
- Omento
- Linfonodi
- **Instestino**
- Cuore
- Esofago
- Trachea
- Meningi



Extraskeletal Osteosarcomas in Dogs: 14 Cases

Fourteen dogs (11 females, three males) with extraskeletal osteosarcomas (EsOSAs) were identified. The median age was 11.5 years. The median body weight was 18 kg. The primary sites of the EsOSAs were the spleen (n=6), mammary gland (n=3), lung (n=2), and one each in the skin, axilla, and mesenteric root. The overall median survival time was 74 days. The only factor which was found to be prognostic for survival was the use of chemotherapy (p of 0.02). Cases which did not have chemotherapy were 3.62 times as likely to die a tumor-related death than cases which had chemotherapy. **J Am Anim Hosp Assoc 1998;34:69–30.**

Charles A. Kuntz, DVM, MS
William S. Dernell, DVM, MS
Barbara E. Powers, DVM, PhD
Stephen Withrow, DVM

RS

From the Comparative Oncology Unit (Kuntz, Dernell, Withrow) and the Department of Pathology (Powers), College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, Colorado 80523.

Introduction

Extraskeletal osteosarcomas (EsOSAs) are uncommon tumors in dogs.[1–7] Approximately 34 cases have been reported previously in the veterinary literature. Diagnosis depends on the satisfaction of the following criteria: 1) uniform morphological pattern of sarcomatous tissue that excludes the possibility of mixed mesenchymal tumor; 2) production of malignant osteoid or bone; 3) high mitotic index; and 4) exclusion of osseous origin.[3,5] Previously reported cases have involved the liver,[3,6] esophagus,[5] upper respiratory tract,[5] jejunum,[3,5] lung,[1] retroperitoneum,[2] anal sac,[2] spleen,[4] mammary gland,[3] adrenal gland, eye, testicle, vagina, kidney, and mesentery.[7] Extraskeletal osteosarcomas are malignant tumors with distant metastases occurring in 64% of cases.[5] Survival times with surgery have ranged from one to 175 days, with one case surviving 45 months.[1]

Although histopathological descriptions of EsOSAs exist, the clinical course has not been described completely. The majority of cases reported in the veterinary literature are individual patients, many of which were euthanized at initial diagnosis.[1,2,4–7,[3,6]] The purpose of this study was to describe the clinical features of EsOSA in dogs, with reference to the effect of treatment.

Materials and Methods

Dogs which presented to the Colorado State University Veterinary Teaching Hospital (CSU-VTH) with EsOSAs (according to the previously mentioned criteria) were included in this study. All histopathological samples were evaluated by a single pathologist (Powers). Tumors were classified and graded according to a previously described scale used to interpret histopathological samples from humans with EsOSAs.[11] An attempt to diagnose an osseous primary lesion was made in all cases by nuclear scintigraphy (n=1), necropsy (n=4), and physical examination (n=14) [see Table]. Each case had three-view thoracic radiographs at the time of diagnosis. Medical records were examined for the following parameters: age at presentation, sex, weight, location of primary tumor, radiographic findings, surgical and chemotherapeutic treatments implemented, date and location of metastasis, date of local recurrence, and date and cause of death. One case was lost to follow-up at 223 days after surgery. All other cases were followed to death.

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CASE REPORT

An Unusual Case Report of Primitive Jejuneal Canine Osteosarcoma

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Intestinal
Osteosarcoma

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ABSTRACT

Extraskeletal osteosarcoma (also called extraosseous osteosarcoma or soft tissue osteosarcoma) is a rare primary malignant mesenchymal neoplasm arising in soft tissues with histologic features resembling primary osteosarcoma of bone but without any direct relation to bony structures. It is much rarer than either soft tissue sarcoma or skeletal osteosarcoma. It can produce osteoid, bone or chondroid material. The pathogenesis of this tumor is still uncertain and in humans they are considered both clinically and therapeutically distinct from primary osseous osteosarcoma. In previous studies canine extraskeletal osteosarcoma accounted for 6.09% of all cases of osteosarcoma and was seen only in mammary glands. Very few cases of primary intestinal osteosarcoma have been described in dogs and other species of animals. This report describes a case of primary intestinal osteosarcoma in Cocker Spaniel dog.

Cite This Article as: Leonardi L., Roperto F, Francisinsi MP and Mandara MT, 2012. An unusual case report of primitive jejuneal canine osteosarcoma. Inter J Vet Sci, 1(2): 69-71. www.ijvets.com

INTRODUCTION

Osteosarcoma is a malignant mesenchymal neoplasm of bone composed of malignant osteoblasts producing osteoid and immature bone (Patnaik, 1990, Turrel, 1982). Extraskeletal osteosarcoma and other primitive malignant bone tumors like chondrosarcoma are uncommon tumors in dogs (Campbell JR, 1964, Goda JS, 2011, Kuntz CA, 1998) and other animal species human enclosed (Piscitelli D., 2005, Ruiz Carazo E., 2010, Schena CJ, 1989, Stimson EL, 2000). A thirteen-year old male Cocker Spaniel dog, weighing about 20 kg., was presented with recurrent abdominal pain, associated with symptoms of depression, hypothermia (37°C), pallor, vomiting and diarrhea. Hematology and clinical chemistry revealed anemia (RBC 3.500.000/mcl, hematocrit 23%) and elevated liver enzymes (GPT, GGT, ALT). Ultrasound scan revealed the presence of abdominal fluid and a globular calcified mass of 7.0 x 8.0 x 6.5 cm. that appeared to be associated with spleen and small intestine. Plain abdominal radiographs (LL and VD projections) confirmed a hyperdense 7.0 x 8.0 x 6.5 cm. mass in the right side of the abdomen showing irregular borders and multifocal areas of calcification. No other lesions were detected in the skeleton or elsewhere in the soft tissue. Exploratory laparotomy revealed a 7.0 x 8.0 x 6.5 cm. intramural tumor that involved approximately 6 cm of the proximal jejuneum. Other findings at surgery included hemoperitoneum and slight hepatomegaly. The remaining abdominal organs appeared grossly normal. The tumor was totally excised along with the involved segment of the intestine and regional lymph nodes, and sent for histopathological examination.

MATERIALS AND METHODS

The tumor was sectioned grossly, fixed in 10% neural buffered formalin, decalcified and embedded in paraffin. Sections of 4-5 µm were cut and stained with hematoxylin-eosin (HE). Immunohistochemistry (IHC) was performed using avidin biotin complex (ABC) method. The following primary antibodies were used: polyclonal anti-human CD117 (c-kit) (1:200; Dako, Denmark), monoclonal mouse anti-vimentin (1:250; clone V9; Dako, Denmark), and polyclonal rabbit anti-S-100 (1:1000; Dako, Denmark). 3-amino-9-ethylcarbazole (AEC Substrate-Chromogen, Dako, Denmark) was used as a chromogen and Carazzi's hematoxylin as a counterstain. Negative controls were performed in the same manner, omitting the primary antibody.

Extraskeletal Osteosarcomas in Dogs: A Retrospective Study of 169 Cases (1986–1996)

Extraskeletal osteosarcomas (EOSs) are rare tumors that arise in various soft-tissue sites (e.g., gastrointestinal tract, subcutaneous tissue, spleen, liver, skin, kidney, urinary bladder, muscle, thyroid gland, eye, and mammary glands). Soft-tissue osteosarcomas (STOs) occur in older dogs with no sex predilection; beagles and rottweilers are at higher risk. Mammary gland osteosarcomas (MGOs) occur in older females; mixed-breed dogs, German shepherd dogs, and miniature poodles are at higher risk. The median survival time for cases with STO was 26 days, and the major cause of death was local recurrence (82%). The median survival time for cases with MGO was 90 days, and the major cause of death was pulmonary metastasis (62.5%). **J Am Anim Hosp Assoc 1998;34:115–20.**

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Introduction

Osteosarcoma is a malignant mesenchymal neoplasm, characterized by the formation of osteoid. It is the most frequent primary bone tumor in dogs, accounting for 85% of all reported bone tumors.[1–3] The skeleton (appendicular and axial) is involved most commonly.[2–4] Extraskeletal osteosarcoma (EOS) is a malignant, osteoid-producing, mesenchymal neoplasm without primary periosteal or bone involvement. Extraskeletal osteosarcoma has been described less frequently.[5–8] Four retrospective studies have been performed previously; three of the studies described characteristics of 32 cases with splenic EOS exclusively, and the other reviewed the histopathological features of 11 cases with EOS.[5–8] The results of these studies have offered only limited information about this rare tumor and have neglected mammary gland osteosarcoma (MGO). This retrospective study of 169 cases describes the behavior, epidemiology, and prognostic features of canine EOS.

Materials and Methods

Case material was obtained from biopsy records of the Surgical Pathology Service at the Veterinary Hospital of the University of Pennsylvania (VHUP). The records from all biopsies with a diagnosis of canine osteosarcoma for a 10-year period (September 1986 through February 1996) were reviewed. Cases with a histological diagnosis of osteosarcoma that had skeletal involvement were excluded. Cases with EOS that had concurrent periosteal or skeletal osteosarcoma at the time of diagnosis also were excluded. Information about size, age, breed, and sex of the dog and tumor location was obtained from the biopsy reports. Additional information, such as body weight (kg), clinical signs prior to presentation, presence of lymph-node or pulmonary metastasis, treatment, and survival time, was obtained from telephone interviews with referring veterinarians and owners, the VHUP clinical records, or both. Data was summarized using means and medians for continuous data and frequency and percentages for categorical data. Data was analyzed by the Student's *t*-test for con-

Vet. Pathol. 27:46–55 (1990)

Canine Extraskeletal Osteosarcoma and Chondrosarcoma: a Clinicopathologic Study of 14 Cases

A. K. PATNAIK

Departments of Pathology, The Animal Medical Center, New York, NY

Abstract. Canine extraskeletal osteosarcomas are extremely rare tumors. Over a period of 25 years at the Animal Medical Center approximately 1,000 cases of skeletal osteosarcomas have been diagnosed. During the same period 11 cases of extraskeletal osteosarcomas and three extraskeletal chondrosarcomas were diagnosed. Tumors of the mammary gland were excluded. Extraskeletal osteosarcomas were found in the adrenal gland, eye, gastric ligament, ileum, kidney, liver, spleen, urethra, and vagina. The chondrosarcomas were found in the mitral valves, lungs, and urethra. The mean age of the dogs with extraskeletal osteosarcoma was 11 years, and the mean age of the dogs with extraskeletal chondrosarcoma was 14 years. The sizes of the tumors ranged from 1 cubic centimeters to 8,312 cubic centimeters. Osteoblastic osteosarcomas were the most common histologic type (7/11, 62.6%); there was a single case of each of the following: fibroblastic, fibrous histiocytic, chondroblastic, and mixed osteo-chondroblastic osteosarcoma. Two of the dogs with chondrosarcomas had synovial mesenchymal chondrosarcomas involving the lungs and omentum. The remaining dog had a regular chondrosarcoma involving the mitral valve. Distant metastases were present in seven of 11 dogs with extraskeletal osteosarcoma and in none of the dogs with chondrosarcoma. In contrast to human beings, in which most extraskeletal osteosarcomas occur in the soft tissues and the extremities, most canine extraskeletal osteosarcomas develop in the visceral organs.

Key words: Chondrosarcoma; dog; osteosarcoma extraskeletal.

Extraskeletal osteosarcomas are mesenchymal neoplasms of soft tissues and visceral organs that produce osteoid and have no involvement of bone or periosteal tissue. They are rare in the dog (Table 1).[1,3,4,6,9,11,12,15,17,19,21] Fifteen cases mentioned by Jacobson[9] were eliminated from this review because of inadequate clinical and histopathologic information. The remaining reports are of single cases, with two exceptions; one describes two tumors of the upper respiratory tract[3] and the other six tumors of the lower respiratory tract.[1] Extraskeletal chondrosarcomas are extremely rare, only one case in a dog was found in the literature.[16]

In dogs, mixed malignant neoplasms (carcinosarcomas) that produce osteoid and chondroid are fairly common among mammary gland tumors and rare among thyroid neoplasms but most arise in conjunction with adenocarcinomas. These tumors were not included in this study because of their bimodal histologic content and their assumed origin from the stromal metaplasia of the associated adenocarcinomas. Extraskeletal osteosarcomas of the esophagus in association with parasite infection with *Spirocerca lupi* have been reported in dogs, and these also were excluded from this study.[5,20]

In animals other than dogs, extraskeletal osteosarcomas and chondrosarcomas are extremely rare. An osteosarcoma of the eye and extraskeletal chondrosarcomas of the extremities have been reported in cats.[2,10] An extraskeletal osteosarcoma has been described in a guinea pig.[7] Experimentally produced extraskeletal osteosarcomas have been reported in nonhuman primates.[8]

Extraskeletal osteosarcomas are also extremely rare in human beings.[4,14,18,22] They compose approximately 1.2% of all soft tissue sarcomas and 1.7% to 4.6% of osteosarcomas.[4,13,22] The extremities are the most common site (27% to 63%) for these neoplasms in human beings, but they have been reported in other tissues including the urinary bladder, intestines, liver, thymus, major blood vessels, testis, and retroperitoneum.[4,13,22,23,24,33,34] These tumors are very malignant in human beings; 69% recur locally and 80% metastasize.[13,14,22] A five-year survival rate is reported in 20% to 25% of patients.[4,13,22] Extraskeletal osteosarcomas, also rare in human beings, have been described at various sites.[13,31]

It is now established in human beings that radiation therapy can cause osteosarcoma.[13,32] Since the introduction of radiotherapy for the treatment of cancer in small animals, post-radiation osteosarcoma has also been reported in dogs.[4,25]

In this report we describe the clinicopathologic findings in 11 dogs with spontaneous extraskeletal osteo-

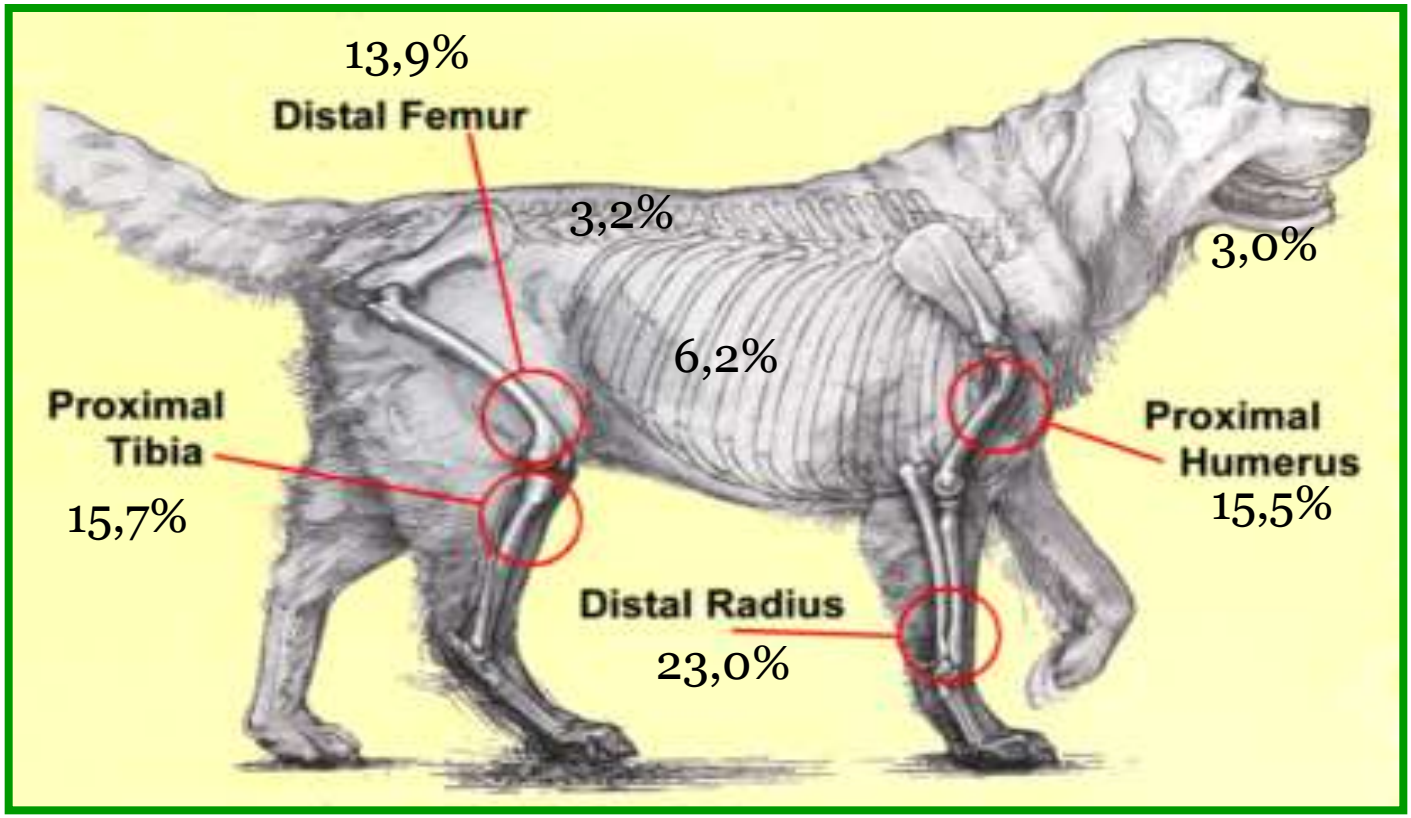
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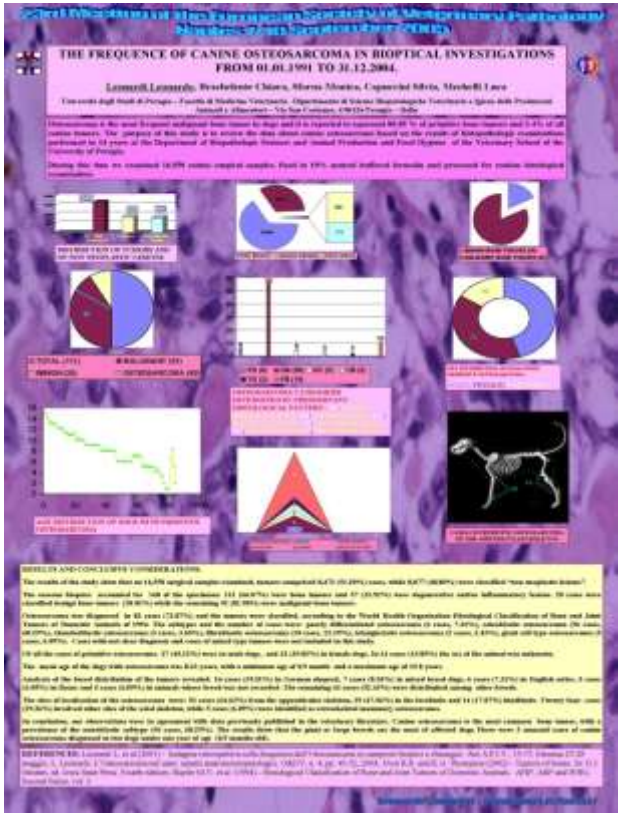
OSTEOSARCOMA canino:

> 80% di tutti i sarcomi primitivi ossei
Razze di grossa mole e giganti
localizzazione appendicolare 75%, localizzazione assiale 25%
arti anteriori (66%) più colpiti dei posteriori (33%)

OSTEOSARCOMA CANINO: 6 ISTOTIPI

OSTEOBLASTICO
CONDROBLASTICO
FIBROBLASTICO
TELANGIECTASICO
A CELLULE GIGANTI
POCO DIFFERENZIATO





CHE COSA ABBIAMO FATTO, COSA FACCIAMO E COSA VORREMMO ANCORA FARE …

- **OSTEOSARCOMA**
- **TUMORE A CELLULE GIGANTI DELL'OSSO**

ISTITUTI ORTOPEDICI
RIZZOLI - BOLOGNA

Istituto Zooprofilattico
Sperimentale
Umbria e Marche

Faculty of Veterinary Medicine Warsaw
University of Life Sciences - SGGW

Universitatea de Stiinte Agronomice
si Medicina Veterinara Bucuresti
Facultatea de Agricultura

CHE COSA ABBIAMO FATTO, COSA FACCIAMO E COSA VORREMMO ANCORA FARE …

Raccolta dei dati e dei casi di tumori spontanei

Classificazione morfologica di tutti i casi

Tipizzazione immunoistochimica di tutti i casi in esame

Caratterizzazione genetica e biomolecolare comparata uomo e animali


American Society for Veterinary Clinical Pathology (ASVCP) 46th Annual Meeting

In conjunction with the American College of Veterinary Pathologists (ACVP) 42nd Annual Meeting

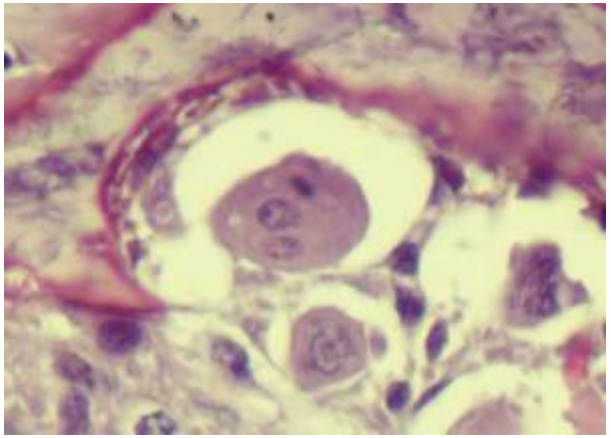
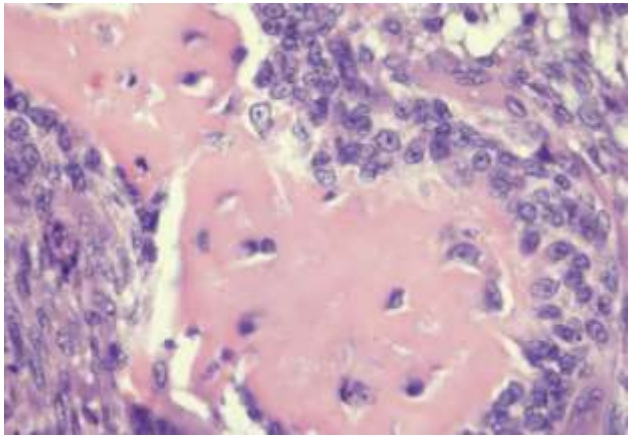


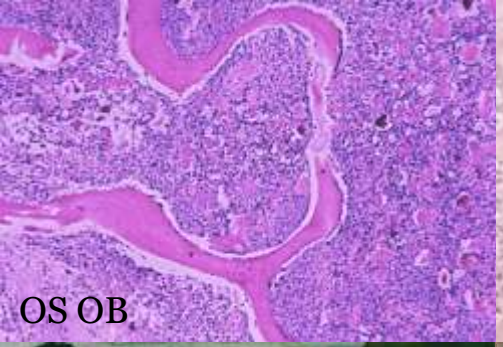


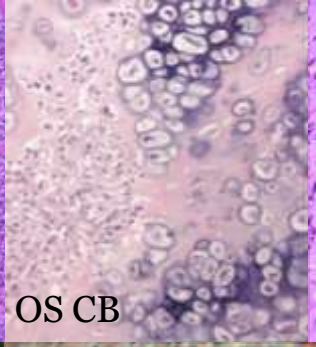


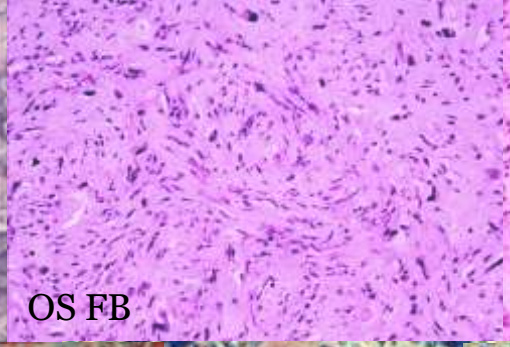

- MMPs
- RANK/RANKL/OPG
- CDK4
- PRb
- P53
- …

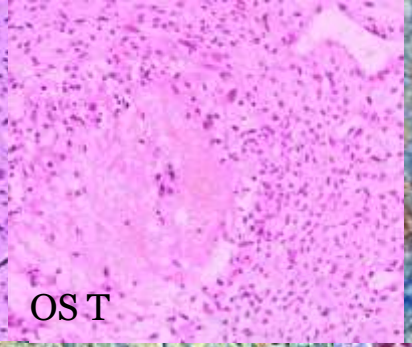
P.R.I.N. 2008
STUDIO BIOMOLECOLARE E GENETICO DELLE CARATTERISTICHE FENOTIPICHE DELL'OSTEOSARCOMA E DEL TUMORE A CELLULE GIGANTI DELL'OSSO, DEL CANE, DEL GATTO E DELL'UOMO

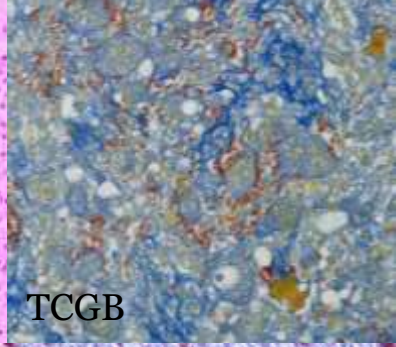





OS OB

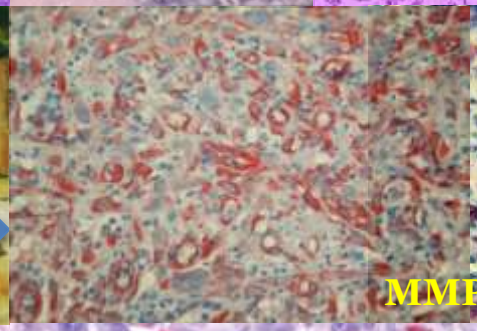

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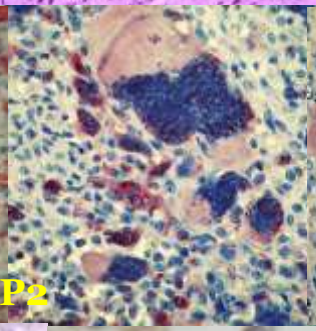

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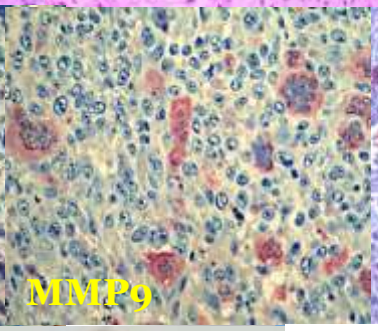

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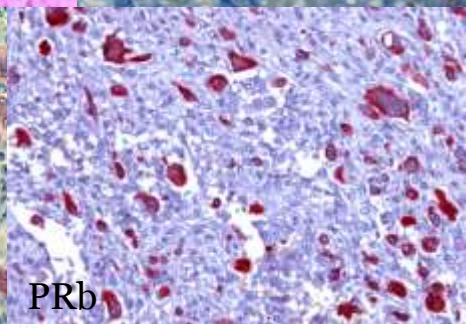

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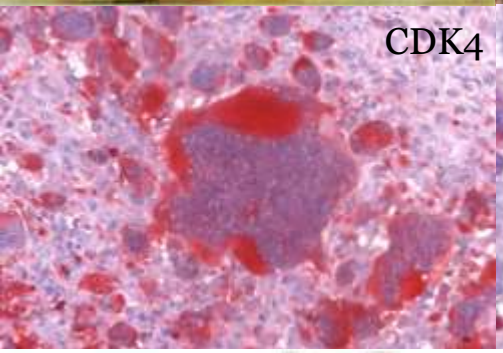

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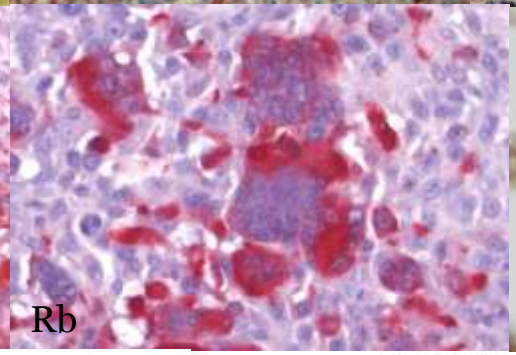

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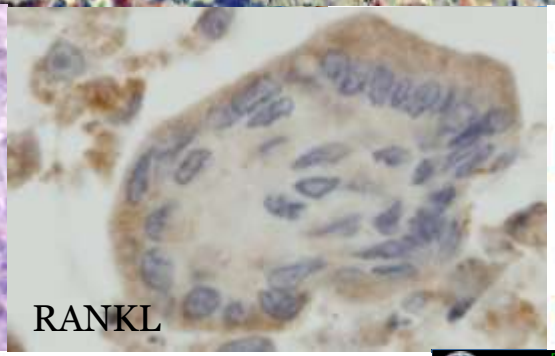


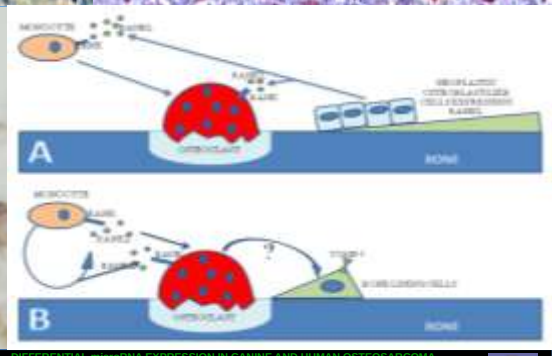

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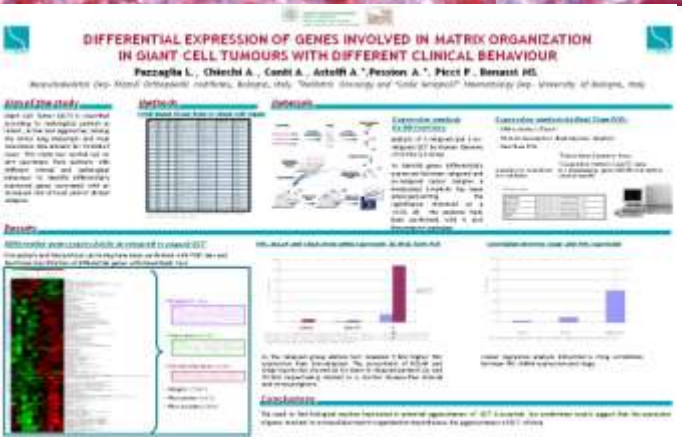

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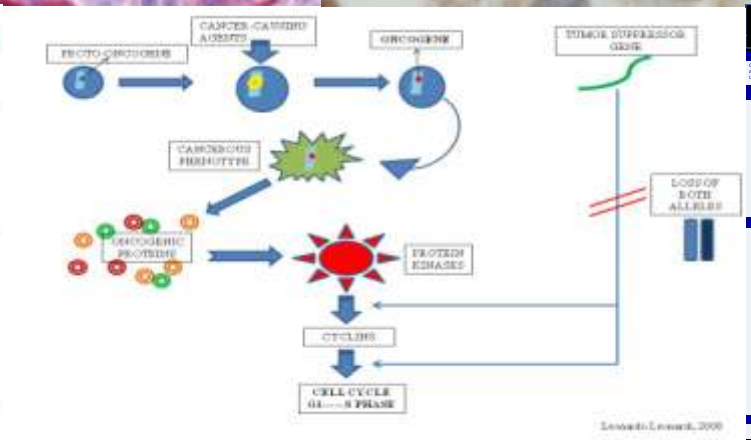

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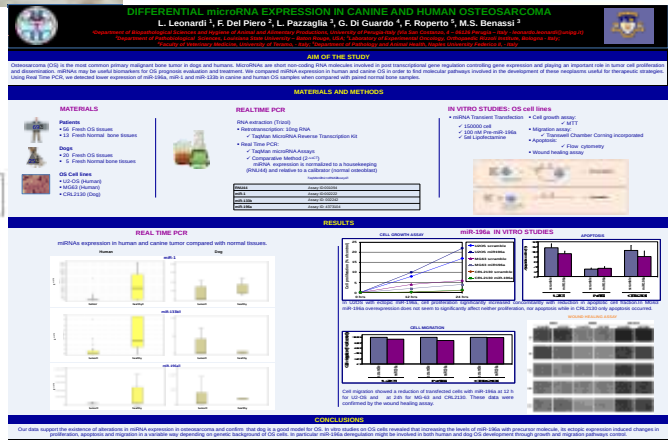

Rb


RANKL


A
B


DIFFERENTIAL EXPRESSION OF GENES INVOLVED IN MATRIX ORGANIZATION
IN GIANT CELL TUMOURS WITH DIFFERENT CLINICAL BEHAVIOUR


CANCER-CAUSING AGENTS
PROTO-ONCOGENE
ONCOGENE
TUMOR SUPPRESSOR GENE
CARCINOGEN INHIBITOR
LOSS OF BOTH ALLELES
ONCOGENIC PROTEINS
PROTEIN KINASES
CYCLINS
CELL CYCLE


DIFFERENTIAL microRNA EXPRESSION IN CANINE AND HUMAN OSTEOSARCOMA
AIM OF THE STUDY
MATERIALS AND METHODS
RESULTS
CONCLUSIONS

RISORSE:



2000 -2013: € 50.000,00

- **Nature Protocols website 2007 (may and july):**





- **Premio Preziosi A.I.P.Vet – Palermo 2008**

... guardando e SPERANDO nel futuro:

L'osteosarcoma (OSA) canino ed umano, modelli biologici in oncologia comparata.
Dal micro-RNA al controllo dei segnali biomolecolari cellulari.

Nessun animale vivo, di qualsiasi specie e razza, è stato mai utilizzato per i nostri studi che si sono sempre avvalsi dell'uso di materiale biologico, prelevato ed utilizzato secondo il totale rispetto delle norme etiche e comportamentali internazionali della Ricerca, da animali colpiti da neoplasie spontanee e trattati sempre in ottemperanza alle Leggi vigenti sulla salute, tutela e salvaguardia degli animali.

La grandezza di una nazione e il suo progresso morale si possono giudicare dal modo in cui tratta gli animali. M. K. "Mahatma" Gandhi (1869-1948)





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