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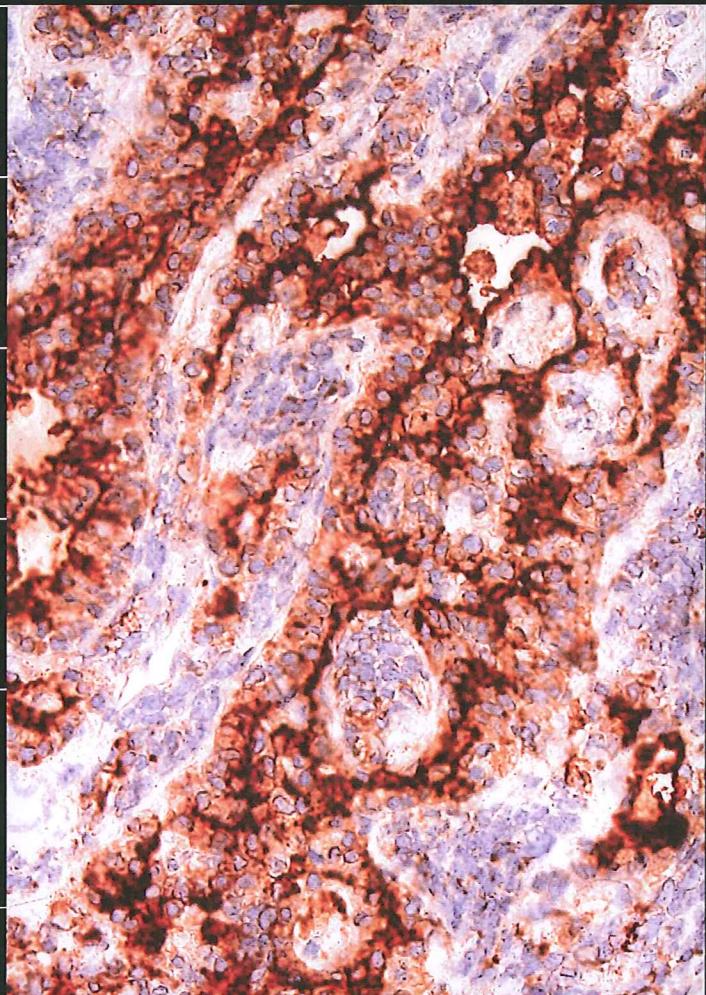
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canine gliomas, which is currently under further investigation. These data provide yet another line of evidence for a close similarity between canine and human gliomas, suggesting that the canines offer a unique, faithful pre-clinical model of human disease.

**MO-16. A SUBSET OF SPONTANEOUS CANINE OLIGODENDROGLIAL TUMORS SHARE GENETIC SIMILARITIES WITH HUMAN OLIGODENDROGLIOMAS**

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Human oligodendrogliomas are characterized cytogenetically by recurrent losses of chromosome arms 1p and 19q. This co-deletion has been associated with a better prognosis and an increased response to treatment. Morphologically similar tumors also arise spontaneously in dogs. Twenty four such cases were identified in the files of the Armed Forces Institute of Pathology (AFIP) with sufficient material for further studies. All available H&E slides were examined by a neuropathologist. Fluorescent in situ hybridization (FISH) studies were performed on paraffin embedded tissues with probes targeting the following syntenic gene regions: HDAC1 (human 1p35.1, canine 2), GLTSCR1 (human 19q13.3, canine 1), and CAMTA1 (human 1p36.3, canine 5). Each FISH probe consisted of three bacterial artificial chromosomes (BACs) which flanked the gene region of interest. Each probe was validated on metaphases obtained from peripheral blood in normal canine controls. A total of 200 non-overlapping nuclei were scored by two independent observers. A third observer evaluated cases with discrepancies. Histologic evaluation revealed that most tumors were high grade and had moderate to high cellularity. Classic oligodendroglial features were present in the majority ( $n = 18$ ), while the remaining resembled oligoastrocytomas or small cell astrocytomas ( $n = 6$ ). The following features were present in decreasing frequency: endothelial hypertrophy ( $n = 18$ ), mucoid background ( $n = 16$ ), increased mitotic activity ( $n = 15$ ), necrosis ( $n = 10$ ), and hemorrhage ( $n = 8$ ). All cases lacked microscopic calcification. Loss of the region of interest was defined as a percentage of monosomy signal of > 60%. Of the 24 cases, 3 (13%) showed loss of GLTSCR1, 2 (8%) showed loss of CAMTA1, and 1 (4%) case showed loss of both GLTSCR1 and CAMTA1. This study suggests that genetic alterations involving chromosomes 1 and 19 previously described in human oligodendrogliomas occur in the syntenic regions of a subset of morphologically similar canine tumors.

**MEDICAL THERAPIES, PEDIATRIC**

**MP-01. A CASE REPORT OF A COMPLETE RESPONSE AND 20-YEAR SURVIVAL OF A PATIENT WITH A RECURRENT DIFFUSE INTRINSIC BRAINSTEM ANAPLASTIC ASTROCYTOMA**

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High-grade diffuse intrinsic gliomas of the brainstem (HDBSG) that recur after radiation therapy carry a grave prognosis and have a median survival of less than 7 months. This presentation describes an unusually lengthy complete response (CR) of a 36-year-old female with HDBSG treated with Atengenal and Astugenal (ANP) which consist of synthetic analogs of naturally occurring phenylacetylglutamine, phenylacetylglutamine, and phenylacetate. The patient was diagnosed with a pontine glioma in June 1987 and biopsy performed on July 25, 1987, at UCSF confirmed an anaplastic astrocytoma. She was treated with hyperfractionated radiotherapy for a total dose of 76 Gy, which was completed on October 9, 1987. In February 1988, she developed diplopia, right facial paralysis and vertigo. A MRI of the head on February 25, 1988, showed interval enlargement of the tumor with extension to the right anterior pons and middle cerebral peduncle. No further therapy was recommended at UCSF due to her tumor progression, and on May 23, 1988, she began treatment with ANP. On May 29, 1988, a low dose of methotrexate 7.5 mg PO daily (0.1 mg/kg/d) in five days on/off courses was added to ANP. On July 12, 1988, methotrexate was discontinued and she continued intravenous infusions of ANP only (the maximum dosage of Atengenal was 0.8g/kg/d and of Astugenal was 0.2g/kg/d). Intravenous ANP were discontinued on August 10, 1989 and replaced by oral ANP (the maximum dosages were 0.14g/kg/d). All treatment was discontinued on January 21, 1990. Follow-up MRIs revealed gradual decrease and eventual disappearance of the tumor on January 23, 1989. Numerous

subsequent MRIs confirmed CR. ANP was well tolerated with only minor reversible side effects including a skin rash, fever and slight leukopenia from which she recovered completely except for a mild right facial nerve paresis, which occurred after the initial tumor biopsy. She is currently doing well and has not suffered from any chronic toxicity related to ANP. Periodical repeat MRIs of the head (the last on April 28, 2007) have shown no tumor recurrence. The National Cancer Institute (NCI) confirmed her diagnosis and CR during a site visit. ANP is a multitargeted therapy, which is currently pending use in Phase III trials in newly diagnosed diffuse intrinsic brainstem gliomas.

**MP-02. VALPROIC ACID IN THE TREATMENT OF MALIGNANT GLIOMA IN CHILDREN**

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Several differentiation inducing drugs are currently tested for their antitumoral activity considering that tumor cells resemble immature precursor cells that can be prompted either to differentiate or to become apoptotic. Previously, we were able to show in preclinical studies that VPA changes the biology of neuroectodermal tumor cells towards differentiation, cytostasis, reduced metastatic capacity and increased immunogenicity. We used the histone deacetylase inhibitor valproic acid (VPA) in the HIT-GBM-C protocol for the treatment of malignant glioma in children. Continuous oral intake of VPA after combined chemotherapy and irradiation for malignant glioma aimed at further reduction of tumor volume or at maintaining the previously achieved remission status after postsurgical combined radiochemotherapy ensuring quality of life. 53 children (32:21 m:f) were treated with VPA. 4 children were treated with VPA for epilepsy and 10 children received VPA despite progressive disease. Median daily dose was 33 mg/kg/day (range: 9.8–78) allowing median trough serum levels of 95 mg/l (range: 24–168). 46 children were evaluable for response to VPA after 6–8 weeks of treatment. 15 patients showed stable disease and 3 children even showed partial remission. Toxicity was mild and patients with tumors responding to VPA treatment had an increased event-free survival. This is the first report showing that the histone deacetylase inhibitor VPA is effective in the treatment of malignant glioma at tolerable drug levels. Thus, we strongly suggest that VPA should be further tested as an antitumoral drug in children.

**MP-03. STABILIZATION FOR 9 MONTHS OF RAPIDLY PROGRESSIVE MALIGNANT GLIOMA USING BEVACIZUMAB, IRINOTECAN, AND TEMOZOLOMIDE IN A PREVIOUSLY HEAVILY TREATED 15-YEAR-OLD FEMALE**

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A 15-year-old female who presented in October 2002 with hydrocephalus and mild left hemiparesis, was found to have a right thalamic area mass for which she underwent a resection. The pathology revealed a glioblastoma multiforme. She also had Gliadel wafers implantation at the time of resection. Her treatments consisted of radiation followed by stereotactic radiosurgery to residual tumor. Chemotherapy treatment consisted initially of temozolomide for 12 months. In September 2005 she developed drop metastasis to the spine for which she had spinal radiation which decreased the tumor size. In January 2006 she initiated irinotecan and cetuximab as part of a clinical trial. In April 2006 there was evidence of progression for which she was enrolled in another clinical trial and she received oxaliplatin in combination with 5-fluorouracil. In June 2006 further progression was identified and at that time Avastin and CPT-11 were started, which stabilized her disease. In November 2006, temozolomide was added with the goal to reduce tumor burden. With this regimen her disease was stabilized for almost 9 months with relative good quality of life. This outcome suggests that using agents with different mechanisms may arrest tumor growth.