Granular cell tumor (GCT), once called granular cell myoblastoma, is a neoplasm of uncertain histogenesis which has been reported in a variety of species [9] including humans, horses, dogs, cats, a ferret, and a cockatiel. GCT in the central nervous system (CNS) has been well documented in humans and rats but has seldom been reported in dogs and other animal species [2–5, 7]. In animals, GCTs located in various tissues are most frequently encountered in rats, dogs, and horses [9, 15]. In rats, GCT is the most common intracranial tumor [11, 15, 20], and the brain, meninges, and pituitary gland are the most common sites. In dogs, GCT most commonly occurs in the oral cavity, but these tumors have also been reported in atypical locations including the brain, heart, and lymph nodes [9]. In horses, the neoplasm has only been reported to occur in the lungs [4, 8]. In cats, GCT has been reported in the tonsil, tongue, vulva, and digits [3, 14]. Human GCT is most commonly located in the tongue and subcutaneous tissue, but various sites may be involved including neurohypophysis or infundibulum [5, 7, 12, 16, 18, 19]. Other reports of GCT in animals included those in the maxillary mucosa in a cockatiel [14] and in the medial portion of the right forebrain in a ferret [17]. Here we report an intracranial granular cell tumor in a dog including magnetic resonance (MR) imaging, pathological, immunohistochemical and ultrastructural characteristics and discuss its possible histogenesis.

A 12-year-old female miniature poodle was presented to the National Taiwan University Veterinary Teaching Hospital with a 3-month history of uncontrolled seizures. Physical examination revealed bilateral cataract, lethargy, and circling to the left. Complete blood count and radiography of the head and thorax showed no abnormalities. Idiopathic seizure was clinically diagnosed and phenytoin (Dilantin®, 22 mg/kg PO q12 hr) and phenobarbital were prescribed pending further examination. Seizures were controlled in the first week of medication. However, seizures, circling behavior, and lethargy recurred one week later. T1-weighted magnetic resonance (MR) image revealed a mass in the ventral pyriform lobe of the right cerebral hemisphere which resulted in compression of the lateral ventricle (Fig. 1). The dog died 3 months after the onset of symptoms.

At necropsy, a 2 × 3 cm white, friable mass was found in the right pyriform lobe (Fig. 2). The tumor mass was well-circumscribed and expansible without encapsulation. The dura meninges tightly adhered to the mass which incorporated the leptomeninges. Additional findings included cataract in both eyes and hepatic nodular hyperplasia confirmed by histological examination. The whole brain was removed, immediately fixed in 10% neutral formalin, and topographically examined. Representative portions of the tumor mass and the adjacent brain tissues were routinely processed for histopathological examination, including hematoxylin and eosin staining. Selected brain sections were also stained with Masson’s trichrome and periodic acid-Schiff (PAS) to detect fibrosis and cytoplasmic granules in the tumor cells. For immunohistochemical (IHC) studies, the avidin biotinylated enzyme complex (ABC) method was used to demonstrate the expression of cytokeratin AE1/AE3 (cytokeratin, 1:50, Dako, Carpinteria, CA), vimentin (1:10, Dako, Glostrup, Denmark), α-smooth muscle actin (1:100, Dako, Glostrup, Denmark), factor VIII related antigen (1:50, Biomeda, Foster City, CA), neurofilament (1:20, Signet, Dedham, MA), and desmin (1:4, Signet, Dedham, MA) using 3,3'-diaminobenzidine (DAB) as a chromogen. For electron microscopic examination, the formalin-fixed tumor tissue samples were placed in glutaraldehyde and following osmium tetroxide, embedded in epon, sectioned at

NOTE

Pathology

Intracranial Granular Cell Tumor in a Dog

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ABSTRACT. A 12-year-old female miniature poodle showed a 3-month history of neurological signs. Magnetic resonance imaging disclosed a high intensity tumor mass in the right cerebral hemisphere with compression of the lateral ventricle. At necropsy, a 2 × 3 cm white, friable mass was found in the right ventral pyriform lobe. Microscopically, the tumor cells were large, polygonal to round cells supported by a sparse fibrovascular stroma. The tumor cells typically possessed finely granular, pale eosinophilic cytoplasm with strongly positive periodic acid-Schiff (PAS) reaction. The tumor cells were immunopositive for vimentin, NSE and S-100. Ultrastructurally, the tumor cells showed large amounts of granules in the cytoplasm, and absence of basement membrane. Based on the above-mentioned findings, the intracranial granular cell tumor was diagnosed.

KEY WORDS: canine, granular cell tumor, intracranial.
Fig. 1. Transverse T1-weighted MR imaging shows hyperintense contrast enhancement (arrows) in the right temporal lobe associated with compression of the lateral ventricle.

Fig. 2. Transverse section at the level of the posterior portion of lateral ventricles shows an infiltrative white granular mass (arrows) involving the neuroparenchyma of the right pyriform lobe.

Fig. 3. The tumor in the right pyriform lobe reveals clusters or sheets of polygonal to round cells and of different sizes with marked cellular borders. The cells show eccentric small to moderately sized, round to ovoid, heterochromatic nuclei with abundant, coarsely granular, pale eosinophilic cytoplasm. HE, Bar=30 µm.

Fig. 4. Clusters of the granular cells with abundant homogeneous cytoplasm (arrow) intermingled with fibroblast-like cells are embedded in the pachymeninges. HE, Bar=30 µm.

Fig. 5. Photomicrograph shows PAS-positive intracytoplasmic granules of the tumor cells after diesterase treatment. PAS. Bar=30 µm.

Fig. 6. Transmission electron micrography shows eccentric nucleus with indented nuclear membrane and a variety of granular structures in the cytoplasm of the tumor cell. The cytoplasmic granules are heterogenous in content. Uranyl acetate and lead citrate. Bar=500 nm.
700 nm thickness, and examined with a transmission electron microscope.

Microscopic examination revealed that the tumor cell proliferation at the base of right pyriform lobe were in the form of clusters or sheets of polygonal to round cells of different sizes with marked cellular borders. The cells often had eccentric small to medium sized, round to ovoid, heterochromatic nucleus with abundant, granular, pale eosinophilic cytoplasm (Fig. 3). They often invaded into the surrounding parenchyma, with clusters of fibroblast-like cells. Mitosis was virtually absent. The tumor cells were embedded and intermingled with the pachymeninges (Fig. 4). Small lobulated arrangement or whorl formation of meningotheelial cells with abundant homogeneous cytoplasm were seen near the tumor border and sometimes in the clusters of the tumor cells. The intracytoplasmic granules of the tumor cells were PAS-positive even after diesterase treatment (Fig. 5). Masson’s trichrome stain showed slight to moderate fibrosis in the tumor. Immunocytochemistry revealed that the tumor cells were immunopositive for vimentin,NSE and S-100, confirming their mesenchymal and neural origin. However, negative results were obtained for GFAP, desmin, α-actin and cytokeratin. Ultrastructurally, the neoplastic cells had eccentric nucleus with invagination of the nuclear membrane and evenly distributed, non-clumped chromatin with 1 or 2 large nucleoli. There was no basement membrane around the neoplastic cells. The cytoplasm was filled with a variety of granular structures. These had heterogeneous contents including round to irregular electron dense structures, finely granular material and vacuoles, presumably phagolysosomes that contained cell debris or cytoplasmic constituents (Fig. 6), as reported previously in animals and humans [3, 5, 13, 16, 19].

The diagnosis of intracranial GCT was established based on the pathological, immunohistochemical and ultrastructural findings of neoplastic tissue obtained at necropsy. GCT in the CNS are well documented in humans and rats but have rarely been reported in dogs [5, 7]. Five cases of GCT in the CNS have been reported in dogs since 1978, and but have rarely been reported in dogs [5, 7]. Five cases of GCT in the CNS are well documented in humans and rats [14, 15]. Most human intracranial GCTs from neurohypophysis are considered to be derived from specialized pituicytes or to originate from Schwann cells or astrocytes [16, 19]. In rats, GCTs are located in or adjacent to the meninges of the cranial cavity, and the histogenesis has been regarded as a progenitor meningotheelial arachnoid cell because of their anatomic location, and immunohistochemical and/or electron microscopic features [10, 11, 20]. An astrocytic origin has been postulated based on positive immunohistochemistry for GFAP, vimentin, and S-100 protein [15]. According to the anatomical and pathological features and ultrastructural characteristics, the present case may suggest a mesenchymal or neural nature.

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REFERENCES