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Case report

Canine intraneural perineurioma

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Abstract

Perineuriomas are slow growing tumors, exclusively compound of well-differentiated perineurial cells. They are rare in human and canine. A dog was submitted to necropsy with a clinical diagnosis of myelin sheath tumor in the brachial plexus area. Slides of the tumor were treated with histochemistry and immunohistochemistry techniches and the diagnostic of perineurioma intraneural was established.

Key Words: peripheral nerve sheath tumors, perineurioma, epithelial membrane antigen

Description

Peripheral nerve sheath tumors (PNSTs) are composed of one or several cellular types including S-100-positive Schwann cells, fibroblasts and perineurial cells in varying proportions. Perineurial-differenciated neoplasms of skin and soft tissues composed predominantly of neoplastic perineurial cells are rare in humans (9) and there are only two reports in dogs (5,7).

Peripheral nerve sheath tumors (PNSTs) have been subclassified rather confusingly in veterinarian literature as neurinomas, neurilemmomas, schwannomas, neurofibromas and neurofibrosarcomas, depending on their presumed cell origin. However, it must be pointed out that such classifications in animals are extremely arbitrary and are based more on extrapolation from human tumors studies rather than on any factual basis of their derivation in animals (8).

Perineuriomas are slow growing tumors, exclusively compound of well-differentiated perineurial cells (6,9,12,12). Two varieties are known nowadays: one a solid and well-circumscribed soft tissue tumor (STP); the other an intraneural proliferation with distinct clinicopathological features, including onion bulb formation - whorls of concentric spindle cells - (6,12), macroscopically characterized by cylindrical segmental enlargement of the peripheral nerves (12). Although the features are different, both share the morphology and immunohistochemical pattern with perineurial cells (11).

In the old days, the term localized hypertrophic neuropathy was used to determine an intraneural variant (1,5,6,9,13). Even though some authors still disregard such condition as a perineurial form, abnormalities in cromossome 22 of STPs and intraneural perineuriomas support the idea that the latter is also a neoplasm of perineurial origin (6).

The clinical signs that indicate perineuriomas are peripheral nerve enlargement (1,6,9,11,12) with the appearance of a circumscribed (9,13), painless, slow growing mass (9,11), and progressive weakness of the limbs (1,5,11), with sensorial and motor deficits (1). Microscopically, it presents as fusiform cell proliferation that forms whorls around a variable number of nerve fibers (onion bulb pattern) (1,5,9,10,12,13) or collagen islands (1); the cell pattern can be reticular (9) or storiform (6,13), with intense collagen fiber proliferation (6,12,13) and abundant mixoid matrix (5,9). Mitoses are rare (6,12) or occasional (13). Cells present bipolar cytoplasm, elongated (5,9,12,13) and palely eosinophilic (9,12) and oval to elongated hyperchromatic nuclei (6,9,12).

A 9-year-old male Beagle dog was presented to the veterinarian with a history of pain in the

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cervicothoracic spinal cord and progressive tetraparesis. The veterinarian suspected of cervical disk displacement and required magnetic resonance imaging. The dog's owner refused to submit the animal and headed it to an acupuncture treatment. The dog went back to the clinic much worse six months later, and died. The clinical diagnosis was myelin sheath tumor in the brachial plexus area.

Tissue obtained at necropsy was fixed in 10% neutral buffered formalin and routinely processed and paraffin-embedded for histological and immunohistochemical analyses. Five-micrometer paraffin sections were stained with hematoxilin and eosin, silver staining for reticulin, luxol fast blue (LFB) for myelin and Masson stain for collagen. Immunohistochemical studies were performed using the streptavidin-biotin peroxidase method (Kit LSAB, DakoCytomation) and polyclonal rabbit antibodies directed against S-100 protein (DakoCytomation; dilution 1:100), glial fibrillary acidic protein (GFAP; DakoCytomation; dilution 1:5000), epithelial membrane antigen (EMA; DakoCytomation; dilution 1:100) and monoclonal rabbit antibody, against vimentin (DakoCytomation; dilution 1:100) and cytokeratin (DakoCytomation; dilution 1:2000).

At necropsy, two nodular masses were seen in the left brachial plexus. They appeared as cylindrical enlargements with 0.8 centimeters of diameter and three centimeters length, one centimeter away from the spinal cord (Fig. 1). The cutting surface of both masses was white and grey striated, covered by a thin capsule. Abreast of the spinal roots, the spinal cord was deformed due to tumor compression, and the spinal nerves were involved.

Fig. 1 – Intraneurial perineurioma, brachial plexus. Spinal Cord and left brachial plexus are involved by the tumor.

With HE staining, the mass was composed of whorl-forming cells, disposed around axons – a proliferation pattern named onion bulbs. The whorls were approximately six cell layers thick and were separated by thin collagen fibers and a few spindle cells. The cells had lightly basophilic elongated nuclei and thin eosinophilic cytoplasm (Fig. 2). Mitoses were not observed. There was invasion of the spinal cord neuropile.

The Masson's method revealed a red color, related to cells and axons. Among the rounded formations, delicate connective tissue stained in blue; the same was better visualized in the transverse sections of the masses (Fig. 3). The capsule was composed of fibrous tissue.

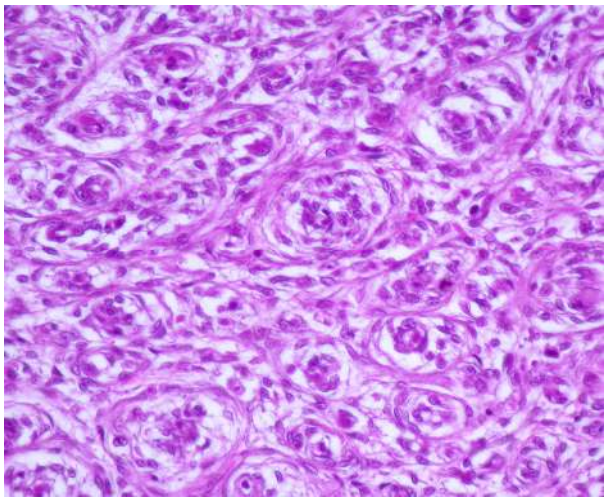

Fig. 2 – Tumor cells have small round nuclei and scarce eosinophilic cytoplasm. HE. Obj. 20x.

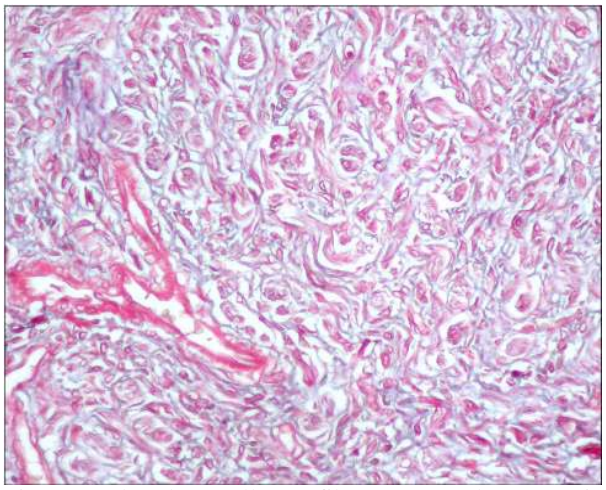

Fig. 3 – Abundant collagen fibers surround concentric cells formation round the axons. Masson's trichrome. Obj. 10x.

Reactivity for S-100 was largely nonspecific, spreading over cells cytoplasm and collagen; the central axons stained positively (Fig. 4). The anti-EMA antibody did not stain in the analyzed sections (Fig. 5). The GFAP and cytokeratin staining were nonspecific. The anti-vimentin antibody stained the vascular endothelium and the tumor cells, in contrast with the central axons, which were negative (Fig. 6).

The first report of canine perineurioma dates from 1974, under the name of localized hypertrophic neuropathy, and it has been demonstrated throughout hematoxilin and eosin and special stains for myelin and axons and electron microscopy (5). The author has attributed the nerve enlargement to Schwann cells

proliferation, collagen fibrillogenesis and prominent intrafascicular accumulations of mucoid tissue. He credited the onion bulb formation to peripheral displacement of excess, non-myelinating Schwann cells in the wake of repeated segmental demyelination, and concluded that the clinical signs, as well as the animal advanced age, remitted to an acquired disease.

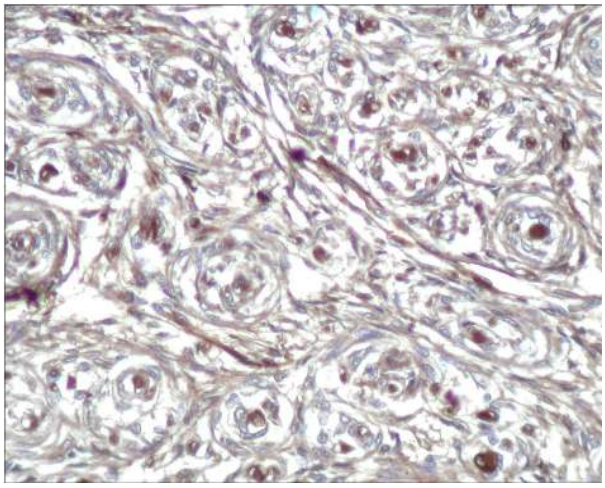

Fig. 4 – Anti-vimentin antibodies label the tumor cells whereas they do not label the central axons. Obj. 20x.

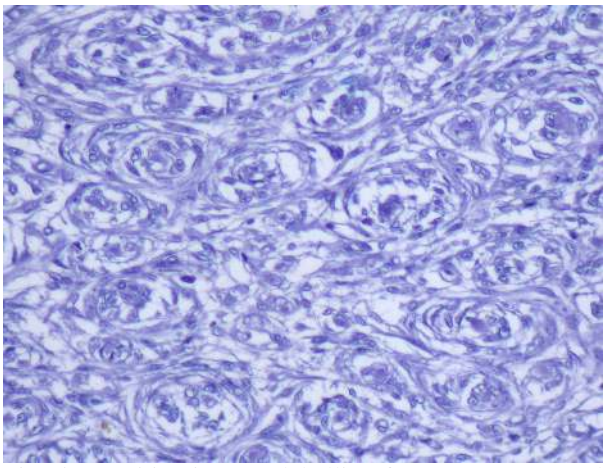

Fig. 5 – Positive immunolabelling for S-100 on central axons and some periaxonal Schwann cells. Obj. 20x.

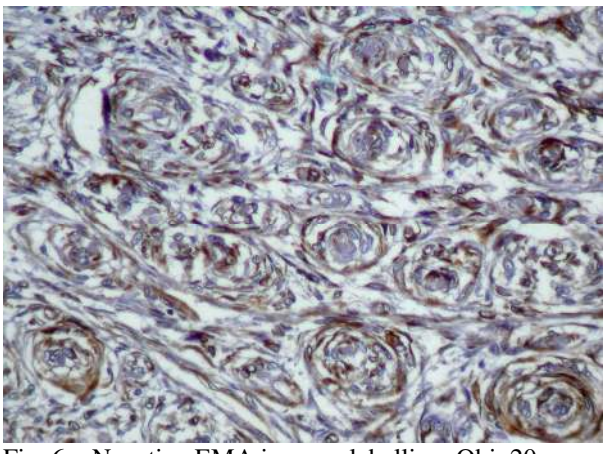

Fig. 6 – Negative EMA immunolabelling. Obj. 20x.

HIGGINGS et al. (2006) recently reported a canine intraneural perineurioma. The dog was a 6-year-old, male German Shepherd Dog, with a history of progressive, non-painful, left pelvic limb paresis. A surgery revealed focally thickened L5 and L6 nerve roots. Light microscopic findings included onion bulb pattern within a mixoid matrix (7). In the present report, the mucoid matrix was scarce and the mass was mostly cellular.

In this case the animal was elder, as well as the foregoing one. In humans, the average age for STPs occurrence is 44 years, within a wide range (1,6,13); the perineuriomas seldom occur in children (9). Toyoda (12) reported perineurioma diagnosis in 11 chicken which were inoculated with an avian leukosis virus, causing the so-called fowl glioma. The animals showed leg paralysis and multiple mild to severe enlargements chiefly in the lumbosacral and brachial plexus and sciatic nerves. In humans, intraneural perineuriomas show up as slowly growing masses (9), with progressive limb muscle weakness (1,5,9) and/or sensory disturbance (1,9). In this case, the patient presented pain in the cervicothoracic spinal cord and progressive tetraparesis.

Cells seen in this case presented similarities with those in other reports. The concentric arrangement around nerve fibers, cells with scarce cytoplasm and elongated nuclei and collagen proliferation remit to perineurial tissue (12). According to Weidenheim (13), the light microscopic appearance of perineurial cell lesions may cause diagnostic problems, and immunocytochemical and ultrastructural features can indicate the tumor cells origin. The ultrastuctural features include numerous evident pinocytotic vesicles and cytoplasmic processes covered by a discontinuous (6,12,13) or continuous basal lamina (7). HIGGINGS et al. (2006) revealed that ultrastructural examination confirmed that the radial pattern of the onion bulbs was formed by concentrically arranged perineurial cells.

According to Perentes (10), while the antibodies anti-Leu 7 and anti-S-100 recognize Schawnn cells and their derivates, the epithelial membrane antigen (EMA) is restricted to perineurial cells (4,9) in the perineurium or as a component of proliferative lesions in the nerve sheaths (10). A recent study revealed positive S-100 immunoreactivety restricted to the centrally placed axons and uniform, strongly positive immunoreactivity for vimentin and laminin on cell processes (7).

Nerve growth factor receptor (NGFR), expressed in the perineurium of normal peripheral nerves and neoplastic Schwann cells, was frequently demonstrated in human PNSTs (4). EMA is considered the most useful stain in human meningiomas diagnosis. Concerning this, Dabbs suggests that the perineurial cells staining throughout EMA may have some value whether investigating neurothekeoma and neurofibroma (3); the author, though, does not display any immunocytochemical panel for perineurioma diagnosis. In the other hand, once the antibodies anti-EMA do not label any antigenic expression in canine tissues (8), and there is no marker for perineurial cells available in the

veterinary field, perineurial origin in canine tumors is difficult to identify (2).

Due to this fact, the description for this tumor in the veterinary literature has often been based purely on histological architecture (2). Stemmer (2004) suggests that ultrastructural confirmation is essential for diagnosis because the onion bulb pattern is not specific and can be seen in other tumors.

In the present report, the diagnosis was based in the light microscopic findings, including routine staining and immunohischemical techniques.

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