Fig. 3. Fibrin thrombus with organization in right basal vein. HE. Bar = 250 µm.

The fresh fibrin thrombus in the midportion of the left basal vein was considered to be responsible for the lesion in the left hypothalamus. The thrombus within the right basal vein was histologically a subacute lesion undergoing fibrous organization, whereas clinical signs, neuropil lesions, and thrombi in the small blood vessels and capillaries were compatible with a more acute process. Such multi-aged thrombi also have been reported in cases of human and nonhuman primates with deep cerebral vein thrombosis. The large venous thrombus in the right basal vein in the present case may have aggravated the hypoxic injury elicited by the acute thrombosis of small blood vessels and contributed to clinical signs and lesions.

References
4 Braund KG, Vandevelde M: Polioencephalomalacia in the dog. Vet Pathol 16:661-672, 1979

Request reprints from Dr. David E. Tyler, Department of Veterinary Pathology, University of Georgia, Athens, GA 30602 (USA).

Naturally Occurring Schwannoma in a Fischer 344 Rat

K. E. LABER-LAIRD, M. P. JOKINEN, AND C. P. JEROME

Tumors of cranial, spinal, and peripheral nerves have been reported in rats treated with chemical carcinogens, but naturally occurring peripheral nerve tumors of rats rarely have been reported. Here we report the gross, histologic, ultrastructural, and immunocytochemical characteristics of a naturally occurring peripheral nerve neoplasm in a Fischer 344 (F344) rat.

A 14-month-old male F344 rat from a commercial supplier fed a commercial pelleted diet ad libitum died 2 months after arrival in the colony with no prior clinical signs. The rat was necropsied, and an ovoid, 3- x 2- x 1-cm, soft, fluctuant nodular mass was located in the caudal mediastinum between the diaphragmatic lung lobes and the diaphragm. The mass was mottled diffusely deep purple to red-black and surrounded the aorta. The cut surface of the mass was deep red-black. The lungs were diffusely red and edematous. The urinary bladder contained red urine, and the mucosal and serosal surfaces of the bladder were hyperemic. There were several punctate yellow foci on the capsular surface of the right kidney, which on section extended as fine pale linear streaks to the corticomedullary junction. The liver was extremely pale and had a marked lobular pattern.

Tissue samples were fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 5 µm, and stained with hematoxylin and eosin (HE). Sections of the tumor were stained with Masson’s trichrome, periodic acid-Schiff, Alcian

blue, and Wilder's reticulin stain. Blocks (1.0 mm³) of the
tumor were rinsed overnight in 2.5% glutaraldehyde in 0.1 M phosphate buffer, post-fixed in 1% phosphate buffered osmium tetroxide, dehydrated in alcohol and propylene oxide, and embedded in Epon B12. Sections were stained with 2% ethanol uranyl acetate and Reynolds lead and examined with a Philips EM 400 at 80 kV. A standard immunoperoxidase technique was used for immunocytochemical demonstration of S-100, glial fibrillary acid protein (GFAP), or neuron specific enolase (NSE) in the tumor. The polyclonal antibodies used were rabbit-derived (Dako/Dakopatts Corp., Santa Barbara, CA). Dilutions for NSE were 1:100, with a human intestinal carcinoid used as the positive control. The dilution used for GFAP was 1:200, and the positive control was human brain tissue. The positive control for S-100 was human salivary gland, and the antibody was diluted 1:150. Negative controls for all three stains were done on rat tissue using normal rabbit sera at the same dilution without the antibody added.

Histologically, the thoracic mass was well circumscribed but not encapsulated. At its periphery, tumor cells infiltrated between and surrounded a few adipose cells and skeletal muscle fibers but did not invade the aorta. The mass was comprised of sheets of loosely packed polygonal to elongated cells arranged in an Antoni Type B pattern, separated by variable amounts of eosinophilic, finely fibrillar matrix (Fig. 1). It was well vascularized. Nuclei ranged from round to fusiform, were hyperchromatic or vesicular, and contained up to two indistinct nucleoli. Mitotic figures were not seen. Many of the cells had scant, eosinophilic, finely granular cytoplasm with distinct borders, while the cytoplasm of the remaining cells was indistinguishable from the surrounding matrix. A few cells had clear, vacuolated cytoplasm. The matrix contained minimal amounts of reticulin and collagen and stained faintly with Alcian blue, indicating a low content of acid mucopolysaccharides. In some areas, spindle-shaped neoplastic cells were seen in the Antoni Type A pattern (Fig. 2). These areas contained moderate amounts of collagen and Alcian blue positive-staining material. The mass also contained numerous irregularly shaped 0.1–5 mm-diameter cysts containing blood or homogenous eosinophilic material and surrounded by densely packed neoplastic cells (Fig. 3). There were scattered foci of hemorrhage, hemosiderosis, and fibrosis. Sections of nerve and a cluster of neuronal cell bodies were seen near the periphery of the mass. Other histologic findings included hepatic biliary hyperplasia, suppurative pyelonephritis, prostatitis, seminal vesiculitis, and hemorrhagic suppurative cystitis.
Immunocytochemistry revealed positive staining cells for both S-100 protein and NSE throughout the mass. The staining intensity of the tumor tissue for these proteins was less than that in the positive controls. Staining for glial fibrillary acidic protein (GFAP) was negative.

Significant ultrastructural features included round to ovoid cells without cytoplasmic processes, intracytoplasmic membrane-bound vacuoles containing osmophilic material, and a continuous basal lamina covering most tumor cells. The extracellular space contained loosely textured fibrillar to granular substance and collagen fibrils.

Diagnosis of collagen-producing tumors as schwannomas depends on several criteria, including: (1) association of the neoplasm with a nerve, (2) presence of Antoni Type A or B histologic patterns, (3) presence of round cells with few cytoplasmic processes, surrounded by a basal lamina, and (4) immunocytochemical confirmation of neuronal origin by demonstration of S-100 or NSE antigens. The primary differential diagnosis is neurofibroma. Although neurofibromas also are associated with neural tissue, they incorporate axons into the neoplasm, whereas schwannomas displace the nerve of origin to the periphery. Neurofibromas contain more collagen and mucopolysaccharides than schwannomas. Cells of neurofibromas may have an external lamina, but also have thin, bipolar cytoplasmic processes. Finally, NSE has not been demonstrated in neurofibromas.

The tumor in this case fulfills diagnostic criteria for schwannoma. The immunocytochemical methods appear to be applicable in the rat, because it has been reported that antihuman S-100 antisera is cross-reactive in the rat, and that S-100 can be demonstrated in similar tissues in both species. NSE has been demonstrated in rat brain, peripheral nerve, and a neoplastic rat Schwann cell line.

Peripheral nerve tumors and histologically similar neoplasms previously described in rats have been termed "malignant neurinomas," or "neurilemmas." Human neurilemmas are now considered to be of Schwann cell origin. In domestic animals, all nerve sheath tumors have been considered variations of a single neoplasm, with "schwannoma" as the preferred term. A Schwann cell origin for rat neurinomas was postulated in one report, based on morphologic and biochemical findings and S-100 positivity. Some reports have designated spontaneous or induced peripheral nerve tumors in rats as schwannomas, based on histologic and ultrastructural characteristics or on ultrastructure and S-100 positivity. The incidence rates for all spontaneous peripheral nerve tumors in F344 rats are low, being reported as 0.05%. Use of all available diagnostic criteria may enable more consistent classification of peripheral nerve tumors in rats and assist in determining their prevalence.

Acknowledgements

This work was supported by NIH grant RR00919 and NIH training grant RR07009.

References


Request reprints from Dr. Kathy E. Laber-Laird, Department of Comparative Medicine, Bowman Gray School of Medicine of Wake Forest University, 300 South Hawthorne Road, Winston-Salem, North Carolina 27103 (USA).