The Ultrastructure of Bovine Peripheral Nerve Sheath Tumours

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Abstract. Bovine peripheral nerve sheath tumours from 30 cattle were similar ultrastructurally to human schwannomas and neurofibromas. Bovine neurofibromatous tissue had large amounts of extracellular material, primarily collagen and electron lucent granular material. The principal cells had basal laminae and a disorganized proliferation of the plasmalemma. Axons were consistently seen and were surrounded by the plasmalemma of principal cells. The principal cells seemed to be Schwann cells or variants of them. Bovine schwannomas had areas similar to Antoni type A tissue with sparse extracellular material, few, if any, axons, and an apparent organized layering of cytoplasmic processes clad in a basal lamina. Cell nuclei often formed palisades. The principal cells in bovine schwannomas might be derived either from Schwann cells or perineurial cells. Bovine schwannomas appeared together with bovine neurofibromatous tissue in affected nerves.

The ultrastructural characteristics of human peripheral nerve sheath tumours have been studied extensively [2, 9, 14]. In human neurofibromas the principal cells have a basal lamina and often are associated with non-myelinated axons. The intercellular material consists primarily of collagen with electron lucent granular material. Other parts such as blood vessels, fibroblasts and mast cells all look ultrastructurally normal. The ultrastructure of human schwannomas is similar to that of neurofibromas. Axons infrequently are seen, however, and generally the cytoplasmic processes of the basal lamina clad principal cells are organized in layers (Antoni type A tissue). Occasionally less organized areas are seen (Antoni type B tissue). Cytogenesis in human benign peripheral nerve tumours has long been debated. Some pathologists say the peripheral fibroblast is the cell of origin [10] but others say it is the Schwann cell [5, 14]. There are, however, few reports on the ultrastructure of bovine peripheral nerve sheath tumours [4, 13]. Ultrastructural similarities to human nerve sheath tumours have been reported [4], and the Schwann cell has been called the principal cell [4].

Materials and Methods

Tumours from 30 cattle were collected from New South Wales abattoirs. Tissue was fixed within 1 1/2 hours after death. Tissue for ultrastructural study was either from diffusely affected nerve or from well circumscribed macroscopic yellow-grey nodules within affected nerve. Several samples were taken from the affected nerve or nerves.
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Fig. 1: Palisading nuclei from area resembling Antoni type A tissue.

Cubes, 1 to 5 millimetres, of tissue were fixed for 1 to 24 hours in 5% glutaraldehyde buffered to pH 7.3 with sodium cacodylate. They then were fixed for 1 to 2 hours in 1% osmium tetroxide and stained for 1 hour in 1% aqueous uranyl acetate. Dehydration was done with graded concentrations of acetone. Infiltration and embedding were done with Spurr’s resin.

Thick sections (1/2 to 1 micrometre) were stained with toluidine blue, pH 11. Thin sections (gold-silver) were placed on Formvar carbon-coated 200 mesh grids and stained with Reynold’s lead citrate [11].

Results

Thick sections from macroscopic yellow-grey nodules had the characteristics of schwannomas. Areas resembling Antoni type A tissue were common and were selected for ultrastructural study. The cells usually were arranged in whorls or sheets with nuclei often in palisades (fig. 1). Cytoplasmic extensions from these cells provided the bulk of tissue and were usually in parallel arrays. The principal cell usually had a nucleus with an irregular but roughly oval outline and indentations and pseudoinclusions (fig. 2). Cytoplasmic organelles were usually sparse and generally included mitochondria, free ribosomes, dilated rough endoplasmic reticulum and pinocytotic vesicles. The plasmalemma was coated with a basal lamina. Axons were rare. Cells resembling fibroblasts occasionally were seen in the Antoni type A tissue. They were distinguished from principal cells by their abundance of cytoplasmic organelles and lack of basal laminae. Intercellular material was sparse and mainly collagen with a periodicity of $640 \times 10^{-7}$ millimetres. Vessels looked ultrastructurally normal.

Areas resembling Antoni type B tissue were difficult to find. Occasionally at the margins of Antoni type A tissue a less organized arrangement of basal lamina clad.
Fig. 2: Area typical of Antoni type A tissue. Principal cell nuclei are roughly oval and a few have indentations (arrow). Cell cytoplasm has few cell organelles. Intercellular material sparse and primarily collagen.
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cells with various amounts of intercellular collagen and electron lucent granular material were seen.

In sections from diffusely thickened nerves there were a variety of areas. There was tissue resembling Antoni type A, but disorganized neurofibromatous areas of scattered cell processes embedded in collagen and electron lucent granular material were more common.

Some areas had “onion bulb-like” structures that varied in size and composition but had some common characteristics. There were always concentric lamellae of basal lamina-clad cytoplasmic extensions and large amounts of acellular material, either collagen or electron lucent granular material (fig. 3). The presence and position of myelinated and non-myelinated axons varied. Nuclei were frequently in the structures and occasionally there were cytoplasmic processes with no basal lamina.

In densely acellular areas, collagen of 640×10⁻⁷ mm periodicity and electron lucent granular material provided the bulk of tissue. Basal lamina clad cytoplasmic processes were sparse and mixed irregularly with the acellular material. They frequently surrounded structures that seemed to be axons. Often collagen seemed to be engulfed by the plasmalemma (fig. 4). Nuclei of the basal lamina clad cells varied in shape, were often indented, and occasionally contained cytoplasmic inclusions. The cytoplasm mainly contained mitochondria, ribosomes and dilated rough endoplasmic reticulum. Usually organelles were sparse. The plasmalemma had numerous folds and frequently there seemed to be proliferation and detachment of basal lamina-like material (fig. 5). Occasionally cells that resembled fibroblasts were seen.

In areas with less acellular material, basal lamina clad cells usually were surrounded with axons, both myelinated and nonmyelinated. Compared with normal nerve, differences were not prominent except for the apparent elongation and folding of mesaxons which divided cell cytoplasm into numerous compartments (fig. 6).

In all areas examined blood vessels had no abnormalities. Plasma cells and lymphocytes frequently were seen scattered in the tissue and surrounding blood vessels. Mast cells were common.

**Discussion**

The ultrastructure of bovine peripheral nerve sheath tumours is similar to that in man. Bovine schwannomas primarily consisted of Antoni type A tissue which is common in human schwannomas. Bovine neurofibromatous areas, as seen in diffusely affected nerve, were similar to those in human neurofibromas. A feature of the bovine neurofibromatous tissue was areas similar in organization to Antoni type A tissue, not usually described in the human condition.

In human schwannomas and neurofibromas a long-spaced fibrous collagen with a macroperiod of about 1200×10⁻⁷ mm has been described [3, 12, 14]. The significance of this atypical collagen is not understood. This collagen was not seen
in bovine schwannomas but a similar structure was seen in an “onion bulb-like” structure in a neurofibromatous area.

The problem of the origin of principal cells in peripheral nerve tumours in cattle is similar to that with such tumours in man. In bovine neurofibromatous areas the
Fig. 4: Area of axons, principal cells with indentations and pseudonuclear inclusion (1). Collagen engulfed by cytoplasmic processes (2).
principal cells, because of their basal laminae and associated axons, seem to be derived from schwann cells. The lack of cytoplasmic organelles within the principal cells is similar to that of normal bovine schwann cells [7]. In bovine schwannomas the principal cell could be derived from a Schwann cell but the perineurial cell cannot be excluded. Perineurial cells with basal laminae are in normal bovine perineurium [7] and have, as do the principal cells in bovine schwannomas, numerous pinocytotic vesicles. The problem may be unimportant especially if, as some authors suggest, the perineurial cell and Schwann cell are functional variants of the same cell type [1].

The appearance of bovine neurofibromatous tissue is more like that of a dysplasia than of true neoplasia. “Onion bulb-like” structures and areas resembling Antoni type A tissue are frequent features and it is tempting to suggest that they represent stages in the development of a true neoplasm with the characteristics of a schwannoma. “Onion bulbing” is not an uncommon phenomenon in human peripheral nerve disorders. In chronic neuropathies it is believed that the formation of “onion bulbs” involves an initial loss of myelinated and non-myelinated axons which results in proliferation of Schwann cells with a change in their surface contours [15]. In human peripheral nerve tumours “onion bulb-like” structures are thought to be formed from basal lamina clad cells that differ from normal human Schwann cells [6]. They probably represent a reactive change to slow progressive nerve degeneration [8].

The “onion bulb-like” structures in the bovine neurofibromatous nerve have a structure similar to those described [4]. The concentric rings of basal lamina clad cytoplasmic processes seem to have cell characteristics similar to those described
Fig. 6: Proliferation of plasmalemma has formed many compartments in cytoplasm. Axons (arrow). Stripping of collagen in intercellular spaces has created artefact.

for normal bovine Schwann cells [7]. Axon damage was not seen in the "onion bulb-like" structures. Therefore it could be argued that they more likely represent a dysplastic process than a reactive process secondary to axon damage. With their continued proliferation, layers of cytoplasmic processes clad with basal laminae could be mistaken for Antoni type A tissue.

"Onion bulb-like" structures were not always seen in diffusely affected nerve but areas resembling Antoni type A tissue were. The mode of development of Antoni type A tissue in these nerves could not be determined. It could have been further development of the already heavily compartmentalized Schwann cells by haphazard proliferation of their plasmalemma.

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References


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