Zeitschrift: Schweizer Archiv für Tierheilkunde SAT : die Fachzeitschrift für Tierärztinnen und Tierärzte = Archives Suisses de Médecine Vétérinaire ASMV : la revue professionnelle des vétérinaires

Herausgeber: Gesellschaft Schweizer Tierärztinnen und Tierärzte

Band: 132 (1990)

Heft: 8

Artikel: Application of immunohistochemistry in canine neuro-oncology

Autor: Ribas, J.L.

DOI: https://doi.org/10.5169/seals-593695

Results

All explants resulted in a confluent monolayer within 2–4 weeks. Syncytia were not observed in explants of lung, mammary gland and choroid plexus of ewe (A). Explants of synovial membrane showed syncytia with the typical circular arrangement of nuclei. Syncytia were detected on the second passage of the cells and increased in number an size with further passages.

Syncytia were consistently present in the explants of mammary gland of the (B) group of ewes but not in explants of lung, synovium and choroid plexus.

The liquid of infected cultures was concentrated (120x) by dialysis against polyethylene glycol, and used as antigen in AGID test against sheep anti-Maedi/Visna positive serum, obtaining a specific precipitation line.

This result, in addition to the biological properties in vitro, permitted to identify the viral isolate as Maedi/Visna virus although comparisons of the nucleotide sequence of the isolate with other ovine lentivirus strains were not performed.

Bacteriological examinations excluded the presence of chlamydia and mycoplasma in the collected tissues.

At necropsy moderate articular lesions with oedema, periarticular carpal tissue thickening, hyperemia and synovial hypertrophy were seen. Induration of mammary gland was ascertained in the animals of (B) group. The lungs did not show the typical changes of lentivirus pneumonitis.

At microscopical examination pulmonary lesions were not seen in any case. Interstitial mastitis with lymphocytes, plasma cells and macrophages arranged in pseudofollicular patterns around galactophorous ducts was evidenced in the ewes of the (B) group.

Articular histopathological lesions were oedema, hyperplasia and hypertrophy of synovium villi and severe infiltration of lymphocytes and plasma cells. Phlogistic cells were also present near the tendon sheaths, sometimes arranged in periarteriolar cuffings. Arteriolar parietal cells were somewhere changed by regressive phenomena. Hyalin degenerative lesions were sometimes ascertained in the connective tissue; necrosis was rare. Recent and older hemorrhagic focal lesions with presence of macrophages filled with hemosiderin were also seen. Frequently were observed few foci of mineralization in the synovium connective tissue. In the semi-thin sections were ascertained syncytia, cytoplasmatic micro-vacuoles and chromatin scattering. Electron microscopy demonstrated mature and budding viral particles morphologically identical to ovi-caprine lentiviruses.

Discussion

Chronic arthritis and synovitis in Maedi/Visna is a rare finding in sheep. We point out in our cases the particular interest of Maedi arthritis with or without mastitis but always without pulmonary lesions as the predominant pattern.

Moreover the virological studies strengthen this observation since the virus was isolated by synovium and mammary gland, but not by lung and choroid plexus explants, with a positive correlation between virus isolation and tissue injury.

References

1. Cutlip R. D. et al. (1985): Am. J. Vet. Res. *46*, 65–68. — *2. Oliver R. E.* et al. (1981): Am. J. Vet. Res. *42*, 1560–1564.

Armed Forces Institute of Pathology, Washington, DC, USA

APPLICATION OF IMMUNOHISTOCHEMISTRY IN CANINE NEURO-ONCOLOGY

J. L. Ribas

In the past twenty years, the identification and biochemical characterization of proteins related to the central nervous system (CNS), coupled with the development of hybridoma technology, have resulted in the development of high specificity anibodies and more refined immunohistochemical methodologies for use with formalin-fixed, paraffin-embedded sections. Nervous system markers include glial fibrillary acidic protein (GFAP), myelin basic protein (MBP), myelin-associated glycoprotein (MAG), S-100 protein, the three subunits of neurofilaments (NF's), and neuron-specific enolase (NSE). In addition, cell markers such as cytokeratins (CK's), vimentin, desmin, oncodevelopmental antigens, photoreceptor proteins (retinal S-antigen and rhod-opsin), Leu-7, B and T lymphocyte surface antigens, Factor VIII-related antigen (FVIII-RA), immunoglobulins, and an array of enzymes, pituitary and hypothalamic hormones, and neurotransmitters have been shown to be useful in diagnostic human neuro-oncology.[1,2]

Among domestic animals, the dog has the highest frequency of primary CNS neoplasms and the broadest spectrum of tumours, the majority of which share morphologic similarities with their human counterparts.[3,4] Although a significant number of these neoplasm are diagnosed with the hematoxylin and eosin stain, approximately 5–10% may be difficult to classify. Reports on immunohistochemistry in veterinary diagnostic neuro-oncology have been relatively few and limited to canine CNS tumours.[5-9] Vandevelde et al.[6] used GFAP, MBP, and MAG antibodies on 74 canine neuroectodermal tumours. Ten of 16 astrocytomas, one of nine ependymomas, two of three glioblastomas, and 9 of 19 poorly differentiated gliomas stained diffusely or focally with GFAP. Oligodendrogliomas reacted with MAG (three out of 11), but not with MBP. In addition to GFAP, canine ependymomas may also stain with S-100, and cytokeratin, the latter marker usually present in anaplastic ependymomas.[7] However, lack of staining of ependymomas with GFAP has been reported.[8] Alpha-fetoprotein have proved useful in the identification of suprasellar germ cell tumours in the dog.[9] Canine choroid plexus papillomas may express epithelial differentiation (three out of 11),[10] but do no stain with GFAP.[6,10] A thoracolumbar spinal cord neoplasm in young dogs with a tendency for epithelial differentiation has been consistently positive for CK.[8,11,12] Staining with vimentin occurs with

meningiomas,[13] and the angioproliferation associated with meningioangiomatosis may be demonstrated with FVIII-RA.[14]

In the past three years, we have applied a variety of neural and non-neural markers to formalin-fixed, paraffin embedded CNS tumours. The most reproducible immunostaining patterns have been cytokeratin for choroid plexus papilloma; GFAP, S-100 and/or cytokeratin for ependymoma; vimentin and/or cytokeratin for meningioma; cytokeratin for thoracolumbar spinal cord blastoma; GFAP for gliomas; and NSE and NF for neuroepithelial neoplasms.

There is considerable variability in the specificity of commercially available polyclonal or monoclonal antisera and, therefore, in their diagnostic value. For instance, GFAP and synaptophysin have an exquisite specificity for cells of the astrocytic and neuronal series, respectively. On the other hand, NSE and S-100 are less specific in their distribution and, therefore, of limited diagnostic value. Also, due to the limited studies that have been carried out with CNS tumours in animals, immunohistochemical results should be carefully interpreted. Lack of staining may be due to fixation or methodological factors, rather than the absence of antigen in neoplastic cells.[1,2,6] The aim of immunohistochemistry is to obtain consistent and highly sensitive results, essential for the confident evaluation of results. The choice of immunohistochemical methods, the inclusion of appropriately selected positive and negative controls, and the implementation of controlled procedures such as optimal incubation times and temperature, dilutions of primary antibody, and requirements for pretreatment of sections with proteases, should be carefully evaluated.

Classification of neoplasms can provide an important estimate of biologic behavior and patient prognosis, and routine histopathology remains the cornerstone of such classification. However, in some instances reliance on morphology alone may be insufficient. Immunohistochemistry have become a powerful research and diagnostic tool in human neurooncology, but its relative value in the diagnosis of primary CNS neoplasms in veterinary medicine is yet to be determined.

References

1. Bonnin JM., Rubinstein LJ. (1984): J. Neurosurg. *60*, 1121–1133. — *2. Russell DS., Rubinstein LJ.* (1989): Baltimore: Williams and Wilkins, pp 657–658. — *3. Luginbühl H.* et al. (1968): Prog. Neurol. Surg. *2*, 85–164. — *4. Fankhauser R.* et al. (1974): Bull WHO *50*, 53–69. — *5. Bilzer T.* et al. (1983): Kong. Dtsch Ges. Neuroanat. Neuropathol. Frankfurt. — *6. Vandevelde M.* et al. (1985): Acta. Neuropathol. (Berl) *66*, 111–116. — *7. Ribas JL.* et al. (1989): Proc. Am. Coll. Vet. Pathol. *40*, 135. — *8. Baumgärtner W., Peixoto PV.* (1987): Vet. Pathol. *24*, 500–503. — *9. Valentine BA.* et al. (1988): Acta. Neuropathol. (Berl) *76*, 94–100. — *10. Ribas JL.* et al. (1989): Vet. Pathol. *26*, 55–64. — *11. Summers BA.* et al. (1988): Acta. Neuropathol. (Berl) *75*, 402–410. — *12. Ribas JL.* (1990): Proceedings, 8th Annual Meeting, Am. Coll. Vet. Int. Med., Washington, DC, p. 1129. — *13. Schulman FY.* et al. (1990): J. Am. Vet. Med. Ass. (in press). — *14. Ribas JL.* et al. (1990): Vet. Pathol. (in press).

Armed Forces Institut of Pathology (AFIP), Washington, DC, USA

COMPARATIVE NEUROPATHOLOGY OF HUMAN (HIV) AND SIMIAN (SIV) IMMUNODEFICIENCY VIRUS INFECTIONS IN MAN AND MACAQUE MONKEYS

J. L. Ribas, H. M. McClure, M. D. Kanzer

The human immunodeficiency virus (HIV) has been etiologically associated with the acquired immune deficiency syndrome (AIDS) in man.[1,2] Involvement of the central nervous system (CNS) by HIV accounts for a significant proportion of the morbidity and mortality associated with HIV infection and AIDS. At necropsy, approximately 75% of HIV patients will have CNS abnormalities caused by opportunistic infections or neoplasms, or as a direct consequence of HIV infection.[3] The simian immunodeficiency virus (SIV) induces in susceptible macaque monkeys an immunosupressive disease which shares common clinical, pathological, and immunological features with AIDS. It is characterized by depletion of the CD4-bearing helper/inducer subset of T lymphocytes, interference with cell mediated immunity, impaired resistance to opportunistic infections, progressive multisystem disease including meningoencephalitis, cachexia, and death.[4]

We have analyzed the comparative neuropathology of late stage disease in 140 adult and 16 pediatric HIV cases from the AFIP AIDS Registry, and acute and late stage disease in approximately 20 young macaque monkeys experimentally infected with several SIV strains. Opportunistic infections constitute the most common finding in adult HIV patients, with more than 50% of cases in our series presenting with one or more reactivation infections.[5,6] A necrotizing encephalitis due to *Toxoplasma gondii* was the most common infectious complication. Reactivation of viral infections due to cytomegalovirus (CMV) and JC virus (a papovavirus) were also commonly seen. CMV can produce in HIV patients a necrotizing ventriculo-encephalitis, polyradiculomyelitis, or a subacute encephalitis, and JC virus is the etiologic agent of progressive multifocal leukoencephalopathy (PML).[6] Opportunistic infections caused by other viruses, protozoa, fungi or bacteria were less commonly seen. Cytomegalovirus reactivation was the main opportunistic infection present in one HIV child with ventriculo-encephalitis and the only CNS infection in one SIV monkey with ganglioradiculitis.

Primary CNS lymphoma is the most common CNS malignancy in HIV patients[7] and was present in our series in 5% of adult HIV patients. Microscopically, it appears as multifocal necrotic masses which are composed of neoplastic B lymphocytes. Although it has been reported in HIV-infected children, it was not present in either children or monkeys in our study.

Over 25% of human patients in our series had evidence of a dementing process during life. Pathologically, when infections or neo-