PRIMARY LEPTOMENINGEAL MEDULLOBLASTOMA: A RARE CLINICOPATHOLOGIC ENTITY

Daniel Hussey, Colleen D'Arcy

Anatomical Pathology Department, The Royal Children's Hospital, Parkville, Vic, Australia

Medulloblastoma is a malignant embryonal neuroepithelial tumour accounting for 20% of childhood brain tumours.¹ Presentation with primary leptomeningeal medulloblastoma without a dominant solid lesion is rare with only 6 previously reported cases.¹ This case series reports $n=3$ further male paediatric patients with primary leptomeningeal medulloblastoma. All cases presented with symptoms of raised intracranial pressure and were initially treated for meningitis. Diagnosis was delayed on average 19 days secondary to equivocal radiology and CSF cytology. Dural biopsy confirmed the diagnosis and revealed anaplastic ($n=2$) and classic ($n=1$) medulloblastoma histology. Molecular subgrouping was consistent with non-WNT/non-SHH (group 3/4) medulloblastoma ($n=3$). Post-treatment follow-up showed clinical and radiological remission in all cases. Our cases are unique as they are the only reported survivors of primary leptomeningeal medulloblastoma to date.

Reference

1. Guo X, Zhong D, Ma W. Primary leptomeningeal medulloblastoma: a rare case. *Clin Neurol Neurosurg* 2012; 114: 1181–4.

ADULT-ONSET SPINAL MUSCULAR ATROPHY WITH SMN DELETION AND ULTRASTRUCTURAL TUBULO-FILAMENTOUS INCLUSIONS IDENTICAL TO INCLUSION BODY MYOSITIS

A. R. W. Kang^{1,2}, M. Davis³, P. Lamont⁴, L. Griffiths⁵, J. Dyke^{1,6}, V. Fabian¹

¹PathWest Neuropathology, Royal Perth Hospital, Perth, WA, Australia; ²School of Medicine, University of Notre Dame, Fremantle, Perth, WA, Australia; ³PathWest Diagnostic Genomics, Nedlands, Perth, WA, Australia; ⁴Neurology and Neurogenetic Department, Royal Perth Hospital, Perth, WA, Australia; ⁵PathWest Electron Microscopic Unit, Nedlands, Perth, WA, Australia; and ⁶School of Medicine and Pharmacology, The University of Western Australia, Crawley, Perth, WA, Australia

Sporadic inclusion body myositis (IBM) is an inflammatory myopathy with the diagnostic criteria on electron microscopy of rimmed vacuoles and 15–18 nm intracytoplasmic/intranuclear tubulofilamentous inclusions. There is a spectrum of neuromuscular diseases with these features and to our knowledge, this is the first case of a genetically proven adult-onset spinal muscular atrophy illustrating inflammation, rimmed vacuoles and tubulofilamentous inclusions.

A 53-year-old male presented at 35 years with slowly progressive weakness, unsteady gait and atrophy of thighs and buttocks.

His upper limbs and distal legs were unaffected. Sensory examination was normal. There was no dysphagia, ocular disturbance, sphincteric involvement and no family history of a neuromuscular disorder. Serum CK was normal. The EMG and deltoid muscle biopsy showed a neurogenic process. Subsequent quadriceps muscle biopsy histology demonstrated denervation and focal myonecrosis, rimmed vacuoles and sarcoplasmic inclusions. Ultrastructurally, rimmed vacuoles with myelinoid phospholipid whorls and degenerate organelles, intracytoplasmic and intranuclear 16 nm tubular filaments were present. Single strand conformational polymorphism (SSCP) showed homozygous deletions of exons 7 and 8 of the SMN1 gene on chromosome 5q.

Our case of genetically proven adult-onset SMA confirms that rimmed vacuoles and 16 nm.

IBM-like tubulofilamentous inclusions occur in a primary denervating condition.

References

1. Dubowitz V, Sewry C, Oldfors A. *Muscle Biopsy: A Practical Approach*. 5th ed. London: Elsevier, 2021.
2. Semino-Mora C, Dalakas MC. Rimmed vacuoles with beta-amyloid and ubiquitinated filamentous deposits in the muscles of patients with long-standing denervation (postpoliomyelitis muscular atrophy): similarities with inclusion body myositis. *Hum Pathol* 1998; 29: 1128–33.

A DETAILED NEUROPATHOLOGICAL ASSESSMENT OF A WESTERN AUSTRALIAN CASE OF BALAMUTHIA MANDRILLARIS AMOEBC ENCEPHALITIS

Jason M. Dyke^{1,2}, Jodi N. White³, David J. Speers^{2,4}, Alexandra R. W. Kang^{1,5}, Vicki A. Fabian¹

¹PathWest Neuropathology, Royal Perth Hospital, Perth, WA, Australia; ²School of Medicine and Pharmacology, The University of Western Australia, Crawley, WA, Australia; ³PathWest Forensic Pathology, QEII Medical Centre, Nedlands, WA, Australia; ⁴PathWest Department of Microbiology, QEII Medical Centre, Nedlands, WA, Australia; and ⁵School of Medicine, University of Notre Dame, Fremantle, WA, Australia

Balamuthia mandrillaris is a protist, amphizoic protozoan that is free-living in the soil. This amoebae can rarely cause cutaneous disease and an amoebic encephalitis, the time-course of which ranges from subacute to fulminant.¹

A 76-year-old male presented with a 1 week history of fevers and rigors, progressing rapidly to weakness with confusion and a GCS of 13 but without localising neurological signs. MRI brain and spine reported diffuse parenchymal and leptomeningeal disease, most marked within the median frontal lobes, favouring an infective/haemorrhagic meningoencephalitis. No causative microorganism was identified on ante mortem investigation. Despite broad spectrum antimicrobial therapies, the patient deteriorated clinically. Brain death occurred 10 days after the initial presentation and the case was referred to the State Coroner's Office of WA.

Post mortem examination diagnosed *Balamuthia mandrillaris* infection which was confirmed by PCR testing of brain tissue and cerebrospinal fluid.

This report details the neuropathological distribution of parenchymal cerebral necrosis, associated with trophozoite and encysted amoebic forms, which suggests a haematogenous portal of entry for the protozoa into the brain. We present detailed neuropathology findings on the third case of *Balamuthia mandrillaris* encephalitis originating in Western Australia to be reported in the literature.

Reference

1. Siddiqui R, Khan NA. *Balamuthia mandrillaris*: morphology, biology and virulence. *Trop Parasitol* 2015; 5: 15–22.

FETAL DYSPLASTIC MEGALENCEPHALY WITH ANGIOMATOSIS AND A PATHOGENIC MTOR MUTATION

A. R. W. Kang^{1,2}, J. E. Dickinson³, B. Kamien⁴, D. Azamov⁵, R. Lakshmanan⁶, J. M. Dyke^{1,7}, V. Fabian¹

¹PathWest Neuropathology, Royal Perth Hospital, Perth, WA, Australia; ²School of Medicine, University of Notre Dame, Perth, WA, Australia; ³Division of Obstetrics and Gynaecology, The University of Western Australia, Perth, WA, Australia; ⁴Genetics Services of Western Australia, King Edward Memorial Hospital, Perth, WA, Australia; ⁵Department of Diagnostic Genomics, PathWest QEII Medical Centre, Perth, WA, Australia; ⁶Medical Imaging, Perth Children's Hospital, Perth, WA, Australia; and ⁷School of Medicine and Pharmacology, The University of Western Australia, Perth, WA, Australia

Dysplastic megalencephaly (DMEG) is a rare cerebral malformation defined by overgrowth and extensive cortical dysplasia of the cerebral hemispheres, usually due to MTOR signalling pathway gene mutations.

A 22 week gestation male fetus was diagnosed with macrocephaly on ultrasound. Subsequent brain MRI demonstrated features of DMEG, including macrocephaly, ventriculomegaly, polymicrogyria, enlarged corpus callosum, enlarged ganglionic eminences and cortical dysplasia. At 35 weeks gestation, the fetus was delivered by caesarean section with a birth weight of 3945 g (>99th percentile). The head circumference was 41cm (>99th percentile) and brain weight 674.5 g (expected 256 ± 70 g). The neonate died at day one of life.

Massive parallel sequencing on amniotic fluid identified a mosaic missense variant in the MTOR gene: LRG_734t1:c.6644=C>Tp.(Ser2215=Ser2215Phe), confirmed by Sanger sequencing. Neuropathology confirmed the neuroradiology findings. On histology dysmorphic neurones, balloon cells, multifocal nodular neuronal heterotopia and focal leptomeningeal glioneuronal heterotopia were identified. Widespread Sturge-Weber syndrome-like features of cerebral and brainstem leptomeningeal and parenchymal angiomas and cortical microcalcification were present.

We describe an unusual case of dysplastic megalencephaly with a pathogenic MTOR mutation, cortical microcalcification and additional Sturge-Weber syndrome-like features in the brain. The Sturge-Weber syndrome-like features have not been reported in DMEG, expanding the neuropathology phenotypic expression of this disease.

References

1. Mirzaa GM, Poduri A. Megalencephaly and hemimegalencephaly: breakthroughs in molecular etiology. *Am J Med Genet C Semin Med Genet* 2014; 166C: 156–72.
2. Jansen LA, Mirzaa GM, Ishak GE, et al. PI3K/AKT pathway mutations cause a spectrum of brain malformations from megalencephaly to focal cortical dysplasia. *Brain* 2015; 138: 1613–28.
3. Mirzaa GM, Campbell CD, Solovieff N, et al. Association of MTOR mutations with developmental brain disorders, including megalencephaly, focal cortical dysplasia, and pigmentary mosaicism. *JAMA Neurol* 2016; 73: 836–45.

DIFFUSE IDIOPATHIC PULMONARY NEUROENDOCRINE CELL HYPERPLASIA (DIPNECH) – A CASE REPORT

Joanna Kang, Karen Whale

Anatomical Pathology Department, Hobart Pathology, Hobart, Australia

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) as defined by the WHO is a generalised proliferation of pulmonary neuroendocrine cells that may be confined to airway mucosa or invade locally forming tumourlets or carcinoid tumours.

We report a case of a female aged 82 who presented with an incidentally detected right upper lobe lung lesion, on a surveillance scan following breast cancer. She had an associated chronic dry cough. Her medical history includes childhood asthma. Preoperative lung function tests were normal. Biopsies of this lesion showed a well differentiated neuroendocrine tumour (carcinoid). She underwent a lobectomy which showed one hilar nodule and one parenchymal nodule. Histopathology showed multiple foci of neuroendocrine cell hyperplasia; as well as a 6 mm carcinoid within the bronchial wall at the hilum, 6 mm carcinoid within lung parenchyma and multiple tumourlets. Although uncommon, this is an important entity to recognise as it is usually treated with steroids, and carcinoid tumours that develop are indolent.

References

1. Travis WD, Brambilla E, Burke AP, et al., editors. *WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart*. 4th ed. Lyon: IARC, 2015.
2. Rossi G, Cavazza A, Spagnolo P, et al. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia syndrome. *Eur Respir J* 2016; 47: 1829–41.

TALL CELL CARCINOMA WITH REVERSED POLARITY – A CASE REPORT

Anurita Kar, Fouzia Ziad

Anatomical Pathology Department, Waikato Hospital, Hamilton, Waikato, New Zealand

Tall cell carcinoma with reversed polarity is a rare subtype of invasive breast carcinoma. Immunohistochemical and molecular research show that it is a distinct entity. It is negative for thyroid specific markers.¹ It also has its own unique molecular mutations