CASE No 8

C. Dunham¹, D. McFadden¹, P Macleod²

¹Department of Pathology and Laboratory Medicine, Division of Anatomic Pathology, Children’s and Women’s Health Centre of British Columbia; ²Department of Pathology, Laboratory Medicine and Medical Genetics, Division of Medical Genetics, Victoria General Hospital

This boy died at six years of age from a profound neurological disorder. His main problems included severe developmental delay and visual impairment and “absent myelination” by MRI. Pregnancy and family histories were unremarkable.

Jitteriness and nystagmus were noted by the nursery staff shortly after birth. After routine discharge, his mother noted abnormal “wobbly” head movements and stiffness in his limbs. Because of hip instability, the boy was triple diaphraged.

By 4 months he had poor weight gain, and despite the placement of a G-tube his weight never exceeded the 10th percentile. At 5 months cortical visual impairment was diagnosed. Over the ensuing months, notes of poor fixation, gaze, tracking and visual inattention were consistently made, although his mother felt that his nystagmus was becoming less noticeable. At 7 months he had no head control. In fact, up until death, he was never able to walk or even sit unassisted, and his head control remained poor.

An MRI of the head at one year of age revealed a thin corpus callosum and “essentially absent myelination”. He could roll from prone to back, but not the reverse. He could push himself up only weakly from the prone position and his limbs were stiff. Language was poor and it remained so until death. No seizures were seen. At age one year there was microcephaly, low central but high peripheral tone with leg “scissoring”. There was generalized weakness and spastic quadriplegia. Deep tendon reflexes were symmetric but brisk (3+), and there was a “crossed” reflex at the knee. Choreoathetoid movements were noted in the arms.

Laboratory investigations were extensive and unremarkable. Notably, genetic testing for PLP and GJC2 (GJA12) gene mutations revealed no mutations.

The patient was reassessed by ophthalmology at age three years. Reduced visual acuity of 20/180 was attributed to dystonic eye movements. There was esotropia during visual interest, bilateral upgoing toes and hand fisting. Terminally he was wheelchair bound with bilateral equinovarus of the feet and tight Achilles’ tendons. Self-aggressive behaviors (lip biting) and excessive drooling were present.

Materials Submitted: 1) H&E/LFB of spinal cord and cerebellum; 2) Digital gross photograph of the cerebrum in coronal section

Question: Diagnosis?