

Ultrasonographic Manifestations of Periventricular Leukomalacia in Preterm Neonates at Teaching Hospital Peradeniya, Sri Lanka

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Abstract—Periventricular Leukomalacia (PVL) is a White Matter Injury (WMI) of preterm neonatal brain. Objectives of the study were to assess the neuro-developmental outcome at one year of age and to determine a good protocol of cranial ultrasonography to detect PVL. Two hundred and sixty four preterm neonates were included in the study. Series of cranial ultrasound scans were done by using a dedicated neonatal head probe 4-10 MHz of Logic e portable ultrasound scanner. Clinical history of seizures, abnormal head growth (hydrocephalus or microcephaly) and developmental milestones were assessed and neurological examinations were done until one year of age. Among live neonates, 57% who had cystic PVL (Grades 2 and 3) manifested as cerebral palsy. In conclusion cystic PVL has permanent neurological disabilities like cerebral palsy. Good protocol of real time cranial ultrasonography to detect PVL is to perform scans at least once a week until one month and at term (40 weeks of gestation).

Keywords—Cerebral palsy, cranial ultrasonography, Periventricular Leukomalacia (PVL), preterm neonates.

I. INTRODUCTION

PERIVENTRICULAR LEUKOMALACIA is an infarction or a haemorrhagic infarction which involves the periventricular white matter of preterm neonatal brain [1]. It is also called Hypoxic Ischaemic Encephalopathy (HIE) or White matter injury of prematurity (WMIP) [2], [3]. PVL occurs in periventricular arterial border zones near the trigones of lateral ventricles and around foramen of Monro near the frontal horns of lateral ventricles [4]. The lesions are usually bilateral and symmetrical [5].

Perinatal hypoxia and ischaemia are main aetiological factors [4]. Fetal or neonatal infections and inflammations are other important aetiological factors [2], [6]. Preterm neonates are affected more often than term neonates because of lack of cerebral auto regulation which is inability to maintain cerebral perfusion with varying systemic blood pressure [4], [7]. Two types of brain injuries, Germinal Matrix Haemorrhage (GMH) and Periventricular Leukomalacia (PVL) occur in the immediate periventricular region. It is the watershed zone between deep and superficial vessels in the preterm neonatal

brain [1], [20]. PVL is the second common type of brain injury and it may accompany GMH which is the more common type [1].

Immature oligodendrocytes which are known as preoligodendrocytes located in periventricular white matter get damaged in PVL [4]. Declining prevalence of PVL occurs after 32 weeks of gestation due to maturation of preoligodendrocytes [4].

There are two types of PVL, cystic and noncystic. The lesions undergo coagulation necrosis [5]. The focal necrotic areas in noncystic PVL are microscopic and evolve into small glial scars rather than cysts whereas focal necrotic areas in cystic PVL are macroscopic and evolve into cysts which are called “Swiss cheese” appearance on cranial ultrasonography [6].

With increasing survival of very premature neonates, the number of survivors with PVL has increased and it is due to the increased duration of exposure to post natal insults like circulatory compromise, Patent Ductus Arteriosus (PDA), Respiratory Distress Syndrome (RDS) and neonatal sepsis [1], [6].

PVL may lead to neuro-developmental delay, cerebral palsy, seizures, visual impairment, sensorineural hearing loss and neonatal deaths [8]-[10]. It is a major health problem which requires additional expenses to the country and also a burden to the patient, family and society.

Though there are various clinical trials of treatment, there is no successful medical treatment for PVL in preterm neonates currently available [4]. Identification of cystic PVL is important to follow up the neonate carefully to decide on early interventions like physiotherapy and multisensory stimulation which may decrease the symptoms and increase motor functions in cerebral palsy [11], [12], [19].

Real time cranial ultrasonography is an effective initial neuro-imaging method which does not involve ionizing radiation, reproducible and can be performed at the patient's bedside [4]. Cranial ultrasonography is useful to predict the neuro-developmental outcome of the neonates with PVL [4], [6].

Objectives of the study were to assess the neuro-developmental outcome of PVL at one year of age and to determine a good protocol of cranial ultrasonography to detect PVL.

II. METHODOLOGY

This is a descriptive study. Two hundred and sixty four

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preterm neonates between 28-34 weeks of gestation admitted to Special Care Baby Unit (SBU) at Teaching Hospital Peradeniya from August 2012 were included in the study. Estimated gestational age (EGA) was taken as the age of neonate but not the period of amenorrhea (POA) as it is not quite accurate. Developmental milestones were assessed from 40 weeks of gestation which is the corrected age [13]. Informed written consent was obtained from the parents of neonates before data collection.

A. Inclusion Criteria

Neonates with risk factors and clinical features of PVL were included in the study. Risk factors are (A) Intrauterine hypoxia due to impaired utero-placental blood flow in pregnancy induced hypertension (PIH), intrauterine growth retardation (IUGR), placenta previa, abruption of the placenta and multiple pregnancies. (B) Intra-partum hypoxia in fetal distress with low Apgar score at birth (less than 5 at 5 min) and resuscitation at birth. (C) Post partum hypoxia in Respiratory Distress Syndrome (RDS), recurrent apnoea, pneumothorax and Patent Ductus Arteriosus (PDA). (D) Infections in prolonged Premature Rupture of Membranes (PROM), chorioamnionitis and neonatal sepsis [4], [7], [9], [17], [18]. The clinical features are nonspecific and those are altered consciousness, abnormal tone, abnormal cry, neonatal seizures, pallor or cyanosis, shock, stupor, coma and decerebrate posturing [5], [8], [14].

B. Exclusion Criteria

Neonates with other causes for neurological manifestations were excluded and those are congenital anomalies including metabolic and genetic causes, congenital infections, meningitis or meningo-encephalitis, recurrent hypoglycaemia and hyperbilirubinaemia, other causes for intra-cranial haemorrhages such as bleeding disorders, birth trauma and other cause for cerebral infarctions due to embolization [1], [6], [15], [16].

C. Real Time Cranial Ultrasonography

Scans were performed through the anterior fontanel of the neonatal head which acts as an acoustic window. A series of ultrasound scans were done for all the neonates, within first 3 days of life, on day 7, once a week until one month and at term. The scans were done by an experienced Medical Officer, Professor of Radiology and Consultant Radiologist using a dedicated neonatal head probe 4-10 MHz of Logic e portable ultrasound scanner. Measurements of lesions and ventricles were documented.

D. Patient Follow Up

Clinical history of seizures, abnormal head growth (microcephaly or hydrocephalus) and developmental milestones were assessed and neurological examinations were done monthly for all babies until one year of age. Monthly ultrasound scans were done for neonates who had PVL. Retinopathy of Prematurity (ROP) was excluded and special investigations like Visual Evoked Potential (VEP) and Brain Stem Auditory Evoked Potential (BAEP) were performed for

the suspected cases which is the normal routine management.

The study was approved by the Ethical Review Committee, Faculty of Medicine, University of Peradeniya. The results were analyzed by SPSS version 14.

III. RESULTS AND DISCUSSION

On cranial ultrasonography PVL initially appears as symmetrically increased periventricular white matter echogenicity ("Flare") with altered echotexture lasting for more than 7 days. Increased periventricular echogenicity lasting for less than 7 days of life is normal [2], [6].

A. Grading System of Periventricular Leukomalacia (PVL)

- Grade 1: increased periventricular echogenicity persisting for ≥ 7 days.
- Grade 2: increased periventricular echogenicity developing into small periventricular cysts.
- Grade 3: increased periventricular echogenicity developing into extensive occipital and fronto-parietal periventricular cysts.
- Grade 4: increased periventricular echogenicity in deep white matter developing into extensive subcortical cysts [2].

Grades 2 and 3 are the cystic type and Grade 1 is the noncystic type of PVL [5], [6]. Grade 4 is mostly seen in full term neonates [2].

Among 264 preterm neonates, there were 21 neonates with PVL and of them 10 had simultaneous occurrence of PVL and GMH.

When considering PVL and PVL with GMH together, there were 8 (3%) neonates with cystic PVL and 13 (4.9%) neonates with noncystic PVL. The incidence of cystic PVL in modern neonatal intensive care units is generally 1-4% [6].

B. Stages of Cystic PVL on Cranial Ultrasonography

Cystic PVL evolves with time and serial scans show four stages [1].

- Stage 1:- Period of increased periventricular echogenicity,
- Stage 2: Transient period of normalization of echogenicity,
- Stage 3: Periventricular cyst formation,
- Stage 4: Resolution of cysts.

Increased periventricular white matter echogenicity manifested within one month of life and lasted for 1-2 weeks duration. Cystic lesions manifested at a variable age ranging from 9 days to 7 weeks of life and persisted for a variable period ranging from 4-10 weeks. There was a period of normal periventricular white matter echogenicity for 1-3 weeks prior to cyst formation.

Increased echogenicity is due to oedema or congestion from the infarction or due to the haemorrhage [3], [6]. Manifestation of anechogenic or hypoechogenic spaces (porencephalic cysts) is due to dissolution of necrotic tissues [1]. Progressive necrosis and gliosis results white matter volume loss and dilatation of ventricles and is called "End stage PVL" [1], [8].

On follow-up cranial ultrasound scans, neonates with Grade

3 PVL had white matter volume loss, ventriculomegaly and prominent extra-cerebral spaces (interhemispheric space, sulci and fissures) indicating cerebral atrophy ("End stage PVL"). Neonates with Grade 2 PVL had only mild ventricular fullness.

Cranial ultrasonography is the first line neuro-imaging method to detect brain injuries in preterm neonates. As PVL evolves with time, series of scans are mandatory to detect lesions [1], [2]. In neonates of 28-29 weeks of gestation cystic lesions will not persist until 40 weeks (term) whereas in neonates of 30-32 weeks of gestation cysts may persist until term. Therefore a series of cranial ultrasound scans at least once a week until one month and at term is a good protocol to detect PVL as mentioned by authors Erick Beek and Floris Groenendaal in an article "Neonatal brain ultrasound, The Radiology Assistant in April 2006 [2].

C. Grading of Hyperechogenicity

Hyperechogenicity in PVL can be divided into 3 grades; Grade 0- less echogenic than the choroid plexus, Grade 1- equally echogenic as the choroid plexus and Grade 2- more echogenic than the choroid plexus [3], [6]. All the neonates who manifested clinically had Grade 2 echogenicity.

D. Differential Diagnosis

Periventricular Venous Haemorrhagic Infarction (PVHI) which is a complication of Grades I, II or III Germinal Matrix Haemorrhage (GMH) categorized as Grade IV GMH is a differential diagnosis. The lesion is usually unilateral and located in the periventricular white matter adjacent to the lateral ventricle and if bilateral it is asymmetrical. With tissue dissolution a porencephalic cyst or cysts which may communicate with the lateral ventricle will be formed [3], [5].

E. Neuro-Developmental Manifestations at One Year

Clinical manifestations evolved with time. Among live neonates, 4 (57%) who had cystic PVL (Grades 2 and 3) manifested as cerebral palsy at one year of age. It is similar to the literature where they have mentioned more than 50% live neonates with PVL manifest as cerebral palsy [2], [5].

At 6 months of age all live neonates (2) who had Grade 3 PVL manifested as microcephaly and spastic cerebral palsy. They had spastic dysplasia or quadriplegia with vision and hearing impairment. At one year of age, 2 out of 5 live neonates with Grade 2 PVL manifested as cerebral palsy and they had hemiparesis or quadriparesis associated with global developmental delay without vision and hearing impairment. None of live neonates with Grade 1 PVL manifested as neurological deficits at the age of one year. (Table I)

Periventricular white matter cysts damage the descending corticospinal or pyramidal tracts, visual and auditory pathways causing motor, vision and sensorineural hearing impairment. Severity of cystic PVL is related to the size and distribution of the cysts [2], [6], [12].

TABLE I
ONE YEAR NEURO-DEVELOPMENTAL MANIFESTATIONS OF PVL

Grade	Total number	Clinical manifestations
1	7	Neonatal deaths-1 Normal- 6
2	2	Neonatal deaths -0 Cerebral palsy-2
3	2	Neonatal deaths -0 Cerebral palsy-2
1 and GMH	6	Neonatal deaths - 2 Normal -4
2 and GMH	3	Neonatal deaths -0 Normal-3
3 and GMH	1	Neonatal deaths -1

Cranial ultrasonography is far from sensitive or predictive in detecting increased periventricular echogenicity and has a sensitivity of only 26% and a positive predictive value of 36%. But serial ultrasound scans has a sensitivity of 75% and specificity of 100% in detecting cystic lesions of PVL [6]. MRI is more sensitive than either CT or ultrasound in detecting PVL and has a sensitivity of 100% and specificity of 79% in detecting lesions [6]. But it needs the sick neonate to be transported to the fixed scan machine which takes long data acquisition time and thus requires sedation and monitoring of the neonate [6].

Neonates with noncystic PVL may have minor motor deficits but prominent cognitive disturbances which manifest in early school age as Attention Deficit Hyperactivity Disorder (ADHD) and learning difficulties which require special educational services. Whether the clinical manifestations are purely due to PVL or due to other associated brain injuries in basal ganglia, cortex and cerebellum is not clear [6]. Therefore MR imaging for the symptomatic children in early school age who had risk factors and clinical features of brain injuries in the neonatal period will be a good future research.

IV. CONCLUSION

When considering Periventricular Leukomalacia (PVL) in preterm neonates, cystic PVL (Grades 2 and 3) has bad prognosis as neonatal deaths or cerebral palsy whereas non cystic PVL (Grade 1) has a good prognosis. A good protocol of real time cranial ultrasonography to detect lesions is to perform scans at least once a week until one month and at term (40 weeks of gestational age).

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