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MR Features of Developing Periventricular White Matter in Preterm Infants: Evidence of Glial Cell Migration

Anne-Marie Childs, Luca A. Ramenghi, David J. Evans, John Ridgeway, Margaret Saysell, Delia Martinez, Rosemary Arthur, Steven Tanner, and Malcolm I. Levene

PURPOSE: MR imaging of the brain is increasingly used in the investigation of the newborn, but little information is available on the normal appearance of the developing brain. We scanned a series of newborn infants in an attempt to define the normal appearance of developing periventricular white matter and to assess how pathologic conditions may modify this appearance.

METHODS: Sixty-eight newborn infants, median postmenstrual age (PMA) 34 weeks (range, 24 to 42 weeks), were subdivided into two groups: group A (n = 33), which included those with normal clinical and sonographic examinations, and group B (n = 35), which contained those with evidence of neuroabnormality detected prior to the MR study, either clinically or by cerebral sonography. Images were acquired in two planes on a 1.5-T imager using turbo spin-echo pulse sequences.

RESULTS: Symmetric periventricular bands of reduced signal intensity were noted in the frontal periventricular white matter on T2-weighted images in 98% of group A infants and in 97% of group B infants. The number of bands was inversely related to PMA. The reduction in number of bands with increasing PMA was delayed in group B infants.

CONCLUSION: The uniform appearance of periventricular bands in a population of healthy infants and their relationship to the infants' maturity is consistent with the results of previous histologic studies. These studies demonstrate the presence of migrating glial cells within the periventricular white matter of infants beyond 20 weeks' gestation, when neuronal migration to the cortex is complete. We postulate that the bands seen on T2-weighted images represent groups of migrating glial cells, providing a further marker of cerebral maturation.

MR imaging is increasingly used in the investigation of newborn infants with neurologic abnormalities. The periventricular and subcortical white matter is particularly vulnerable to hypoxic ischemic insult in the perinatal period. The pattern of resultant injury varies from subtle abnormalities to gross cystic degeneration and abnormal gliosis. To assess the significance of the more subtle lesions, it is essential to define the normal appearance of developing white matter.

The original reports in the literature, which attempted to define normal anatomy, had little data from healthy preterm infants (1-3). Since this early work, MR imaging technology has improved significantly,

enabling the acquisition of thinner sections and providing improved signal-to-noise ratio. In particular, the use of turbo spin-echo pulse sequences, with longer effective echo times, has enhanced contrast within nonmyelinated white matter without lengthening image acquisition time.

Two recent studies assessed myelination and cortical maturation in preterm babies, but did not comment on changes in the periventricular or subcortical white matter (4, 5). The aim of the present study was to determine the normal appearance of these regions of the brain and to identify potential markers of white matter maturation. By selecting two groups of infants, those with and without neurologic disorders, it was hoped to distinguish pathologic from nonpathologic features over a range of gestational ages.

Methods

Patients

To define the normal appearance of developing white matter, we considered it essential to study a population of infants in whom neurodevelopment was believed to be proceeding along a normal course. All the parents of infants admitted to

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From the Centre for Reproduction, Growth and Development, University of Leeds (A-M.C., L.A.R., D.J.E., M.I.L.), and the MRI Department (J.R., M.S., S.T.) and the Department of Paediatric Radiology (D.M., R.A.), The General Infirmary at Leeds.

Address reprint requests to Dr. Anne-Marie Childs, Paediatrics and Child Health, D Floor, Clarendon Wing, The General Infirmary at Leeds, LS2 9NS, United Kingdom.

TABLE 1: Reasons for inclusion in group B (n = 35)

Diagnosis	No. (No. with Abnormal Cranial Sonograms)
Abnormal neurologic assessment with or without systemic malformation	8 (5)
Hypoxic ischemic injury	7 (2)
CNS malformation	6 (6)
Posthemorrhagic ventricular dilatation	5 (5)
Periventricular cysts or persistent periventricular echodensity	4 (4)
CNS infection	3 (1)
Venous infarction	2 (2)

the intensive/special care unit over a given period of time were approached, and the nature of the study was carefully explained to them. The infants whose parents gave their consent were entered in the study. Before MR imaging, the infants were subdivided into two groups, designated as A and B. Group A consisted of those infants with no clinical indication of neurologic abnormality and no evidence of parenchymal injury on cranial sonograms. The remainder of the infants were included in group B (see Table 1). The study was approved by the local ethics committee.

Sixty-eight infants with gestational ages (GA) of 24 to 42 weeks (median, 34 weeks) and birth weights ranging from 0.64 to 4.9 kg (median, 1.91 kg) were imaged at a median postmenstrual age (PMA) of 37 weeks (range, 29 to 64 weeks). GA was assessed from maternal dates and sonograms obtained in early pregnancy. PMA was calculated as GA (weeks) plus postnatal age (weeks).

MR Techniques

All infants underwent the same imaging protocol on a 1.5-T MR unit equipped with a receive-only quadrature head coil. T2-weighted images were acquired in the axial and coronal planes, and corresponding T1-weighted images were acquired in the axial plane. The parameters used for T1-weighted spin-echo images were 800/13 (TR/TE), 180-mm field of view (FOV), 4-mm section thickness with a 0.4-mm gap, and a scan time of 3 minutes 52 seconds. The parameters for T2-weighted fast spin-echo images were 6000/200, echo train length of 13, FOV of 180 mm, section thickness of 3 mm with no gap, and a scan time of 5 minutes 12 seconds.

The infants were not sedated during imaging, which was timed to take place soon after a feeding and included the use of a pillow filled with polystyrene balls, which could be molded around the head by vacuum extraction of air. These precautions allowed most infants to sleep throughout the procedure. The infants were monitored continuously using pulse oximetry and a separate ECG recording. Two trained pediatricians were present at all times.

Analysis

The MR images were assessed by two investigators experienced in MR evaluation who were unaware of the ages of the infants. All images were viewed on a Philips Easy Vision standalone workstation using proprietary software.

Periventricular bands were scored as follows: 0 = no band, 1 = single band, 2 = multiple bands. This scoring system was applied to a single T2-weighted image in each plane. The axial image selected was that nearest the foramen of Monro, and the coronal image selected was the most anterior section on which both temporal lobes could be identified.

TABLE 2: Characteristics of patients in groups A and B

	No.	Median (Range) Gestational Age, wk	Median (Range) Birth Weight, kg	Median (Range) Postmenstrual Age at Imaging, wk
Group A	33	33 (24–37)	1.6 (0.64–3.8)	35 (30–44)
Group B	35	37 (26–42)	1.74 (0.74–4.9)	39 (29–64)

Results

Patients' Characteristics

Thirty-three infants were enrolled in group A and 35 infants in group B. Characteristics pertaining to the subjects in the two groups are given in Table 2. None of the infants experienced adverse events during the scanning procedure.

White Matter Appearance

Group A.—In four infants, coronal images were not acquired and in a further five patients the coronal images were too blurred by movement artifacts to permit analysis. The axial images were of sufficient quality to make an assessment in all but one infant.

A consistent feature noted on T2-weighted images was the appearance of symmetric, low-intensity periventricular bands in the frontal white matter (Fig 1A and C). These were seen on coronal and axial images in 100% and 98% of infants, respectively. Although not as clearly defined, equivalent bands of high signal intensity were seen on T1-weighted axial images (Fig 1B). In all those infants with demonstrable bands, corresponding low-intensity stripes were seen on superior T2-weighted axial images (Fig 1D).

The majority of infants had only one demonstrable band, whereas others had additional narrower bands (Fig 2). To further define these bands and to assess whether there was an association with the maturity of the infants, a simple scoring system was devised, which showed an association between number of bands and PMA (see Table 3). A Mann-Whitney U test was used to compare the subgroups with a score of 1 and those with a score of 2. The test revealed a significant difference in the PMA of the infants in each subgroup, with less mature infants having an increased number of bands ($P = .004$ for scores derived from axial images, $P = .03$ for scores derived from coronal images).

Group B.—In three infants with gross ventricular dilatation and two with extensive cystic periventricular leukomalacia, assessment of the white matter was impossible. In six infants, the coronal images were adversely affected by movement artifacts. The periventricular bands noted in the group A infants were seen in 28 (98%) of the babies in group B, although the usual symmetric appearance was sometimes distorted by other abnormalities (Fig 3).

The PMA of infants with more than one band was not significantly lower than that in infants with a single band (see Table 4). However, the PMA of infants in group B with multiple bands (the subgroup

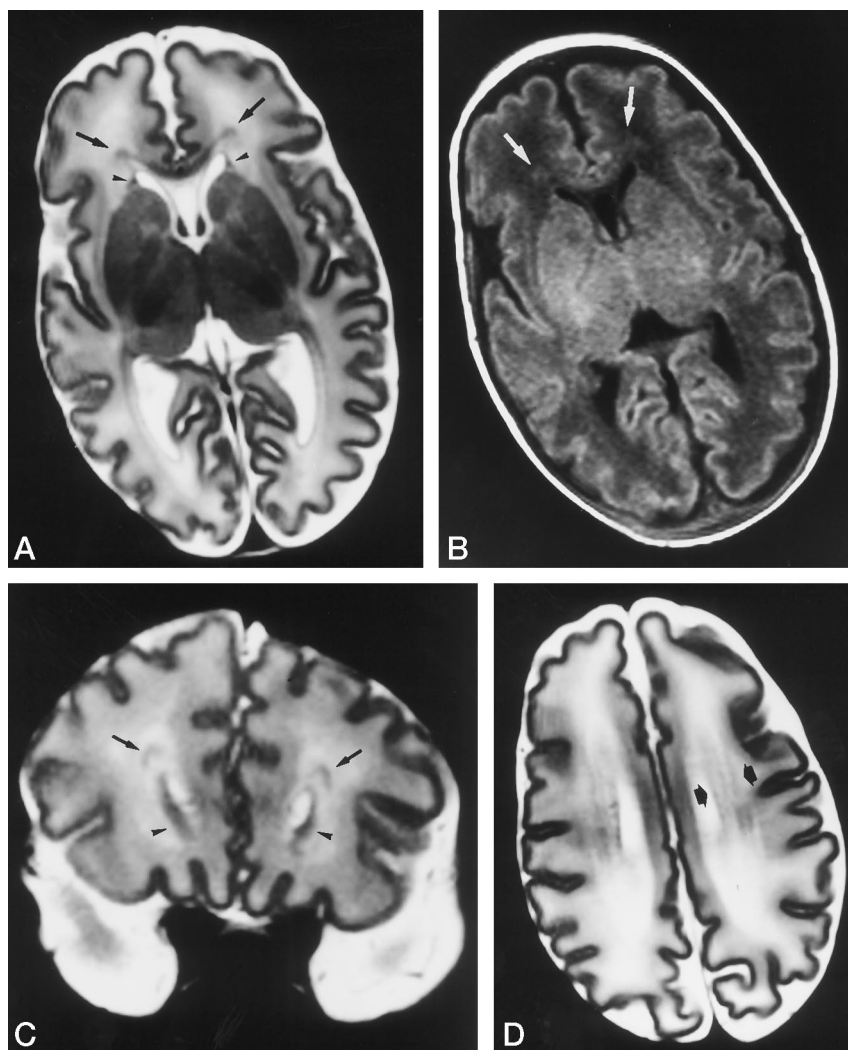


FIG 1. Series of MR images in an infant boy (GA, 30 weeks; PMA, 3 weeks).

A, T2-weighted axial image through the foramen of Monro shows low-signal-intensity periventricular band in frontal white matter (arrows) and germinal matrix at anterior horns of lateral ventricles (arrowheads).

B, Corresponding T1-weighted axial image with poorly defined area of high signal intensity in periventricular region (arrows).

C, T2-weighted coronal image through tip of anterior horns of lateral ventricles shows low-signal-intensity band (arrows) and germinal matrix (arrowheads).

D, T2-weighted axial image through roof of lateral ventricles shows multiple longitudinal low-intensity stripes as bands are transected more superiorly (between arrows).

with a score of 2) was significantly higher than that of infants in group A with multiple bands ($P = .002$ for scores derived from axial images, $P = .02$ for scores derived from coronal images).

Discussion

Ninety-eight percent of group A infants and 97% of group B infants were noted to have a number of low-intensity bands in the frontal regions on T2-weighted images. These corresponded to longitudinal stripes noted on superior transverse images (Fig 1).

The presence of these periventricular bands has been previously described on MR images obtained in infants after birth asphyxia. The authors of that study (6) assumed that the bands were pathologic and postulated that capillary damage and leakage may have produced the appearance. In our study, the prevalence of these bands and their consistent and symmetric nature in a population of clinically healthy infants (group A) would suggest a nonpathologic origin.

The signal intensity of the bands on T2-weighted sequences was similar to that of the subependymal germinal matrix, which was still evident at the caudothalamic notch and proximal to the anterior horns of

the lateral ventricles in many of the infants. This suggests that the bands may represent an area of tightly packed cell nuclei.

The wider band noted on MR images more proximal to the ependyma corresponded to a similar band seen on pathologic specimens (7). This band was the last to disappear and was still evident in three infants born after the 37th week of gestation. The narrower, more peripheral bands on MR images corresponded to populations of migrating cells within the frontal white matter (Fig 4). In the same postmortem study (7), additional bands of migrating cells were noted to radiate from the ependyma to the parietal and occipital cortices in the brains of infants from 20 to 30 weeks' gestation. We postulate that the bands of low signal intensity noted on T2-weighted images in our study represented populations of glial cells migrating through the developing white matter, as the migration of neuronal cells to the cortex is known to be complete by the 20th week of gestation (8). Indeed, histologic studies in human fetuses have recently shown active glial cell migration to the cortex until birth (9, 10).

As the brain matures, more glial cells will have reached their final destination in the cortex or differ-

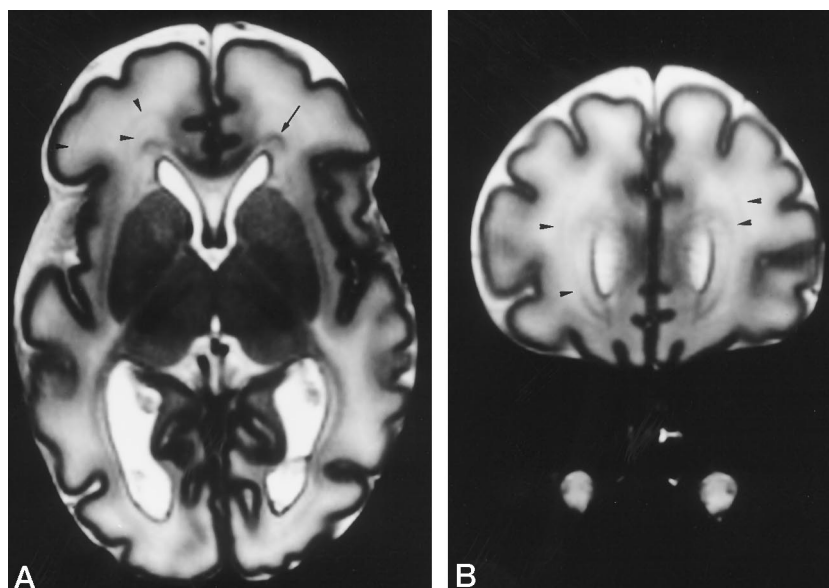


FIG 2. MR images in an infant with a GA of 30 weeks and a PMA of 10 days.

A, T2-weighted axial image through foramen of Monro shows narrower bands (*arrowheads*) situated more peripherally in frontal white matter in addition to the wider band (*arrow*) more proximal to the lateral ventricles.

B, T2-weighted coronal image shows narrower bands (*arrowheads*) evident in the frontal white matter.

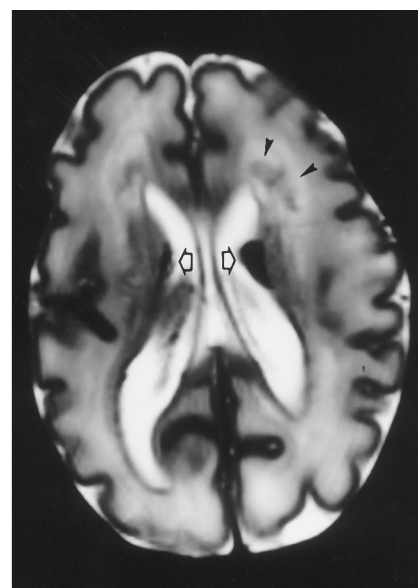


FIG 3. T2-weighted axial image in an infant with a GA of 31 weeks and a PMA of 2 days shows bilateral germinal matrix hemorrhages (*arrows*) in posterior horns of lateral ventricles. The low-signal-intensity band in the periventricular white matter is distorted, particularly in the left hemisphere (*arrowheads*). This was not evident on corresponding T1-weighted image (not shown).

TABLE 3: Image assessment in group A infants

	Axial Image Score			Coronal Image Score		
	0	1	2	0	1	2
No. of infants	1	7	24*	0	5	19†
PMA, median	43	36	35	NA	38	35
PMA, range	NA	36–44	30–39	NA	34–44	30–39
PMA, interquartile range	NA	36–40	32–36	NA	35–42	32–36

Note.—PMA = postmenstrual age expressed in weeks.

* Four of these infants had two additional narrower bands (PMA = 30, 30, 31, and 32 weeks, respectively); one had three additional narrower bands (PMA = 31 weeks); the remainder had only one narrower band.

† One infant had two narrower bands and one had three narrower bands (PMA = 30 and 31 weeks, respectively); the remainder had only one narrower band.

TABLE 4: Image assessment in group B infants

	Axial Image Score			Coronal Image Score		
	0	1	2	0	1	2
No. of infants	2	18	10*	3	14	7†
PMA, median	47.5	39	38.5	52	40	38
PMA, range	43–52	29–64	33–60	43–64	29–54	33–60
PMA, interquartile range	NA	37–42	36–41	43–64	36–41	35–41

* One infant had two narrower bands and one had three narrower bands (PMA = 33 and 31 weeks, respectively); the remainder had only one narrower band.

† One infant had two narrower bands (PMA = 33 weeks) and the others only one narrower band.

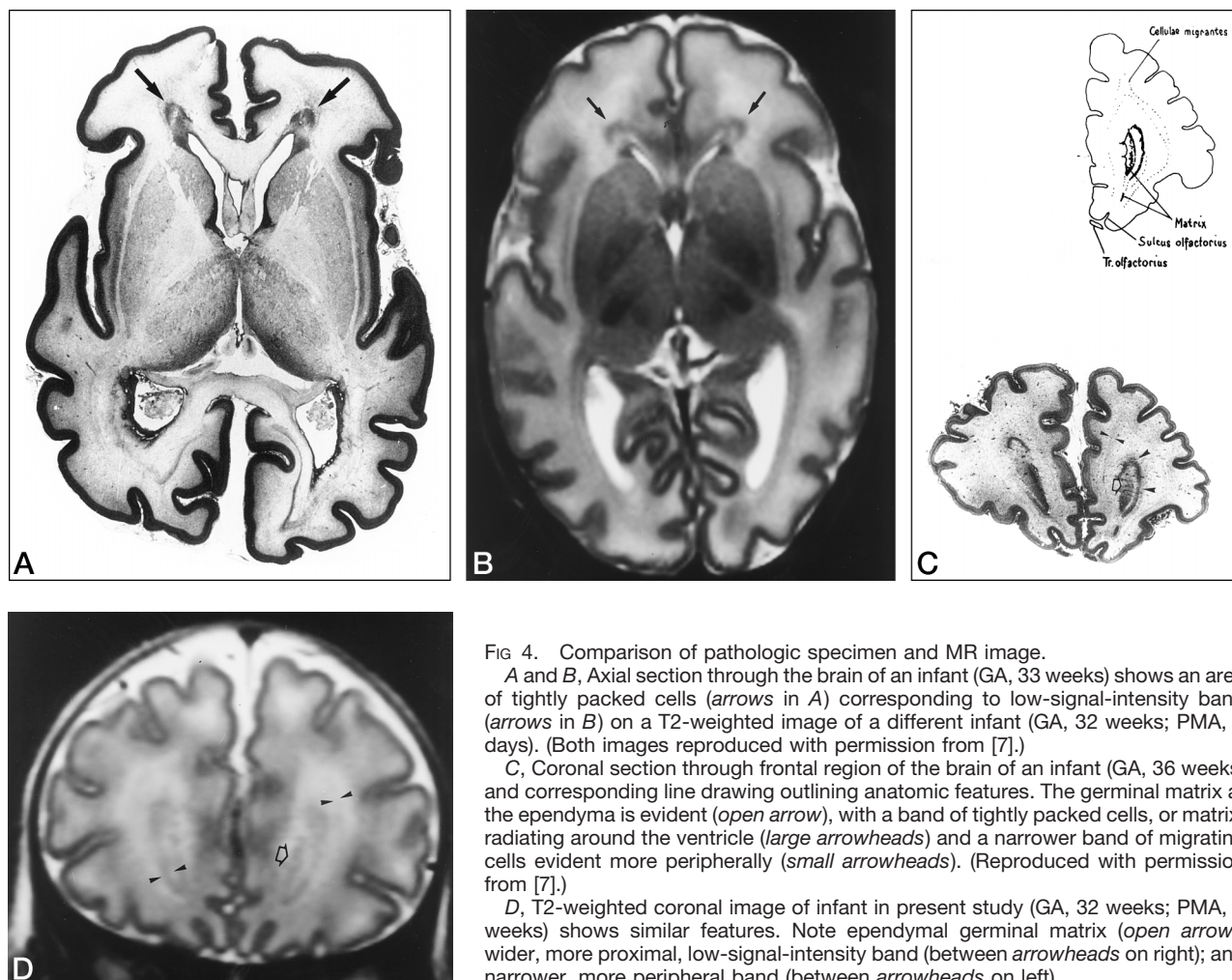


FIG 4. Comparison of pathologic specimen and MR image.

A and B, Axial section through the brain of an infant (GA, 33 weeks) shows an area of tightly packed cells (arrows in A) corresponding to low-signal-intensity band (arrows in B) on a T2-weighted image of a different infant (GA, 32 weeks; PMA, 8 days). (Both images reproduced with permission from [7].)

C, Coronal section through frontal region of the brain of an infant (GA, 36 weeks) and corresponding line drawing outlining anatomic features. The germinal matrix at the ependyma is evident (open arrow), with a band of tightly packed cells, or matrix, radiating around the ventricle (large arrowheads) and a narrower band of migrating cells evident more peripherally (small arrowheads). (Reproduced with permission from [7].)

D, T2-weighted coronal image of infant in present study (GA, 32 weeks; PMA, 3 weeks) shows similar features. Note ependymal germinal matrix (open arrow); wider, more proximal, low-signal-intensity band (between arrowheads on right); and narrower, more peripheral band (between arrowheads on left).

entiated into astrocytes within the white matter (10). This would explain the reduction in the number of bands observed with advancing gestational age. The bands noted on T2-weighted images may represent type II radial glial cells, which migrate horizontally within developing periventricular white matter before they are transformed into fibrous astrocytes (9).

Postmortem studies confirm that the bands of migrating glial cells are only evident in the frontal region of the brain in infants over 30 weeks' gestation, whereas infants of 20 to 30 weeks' gestation also have bands of cells in parietal and occipital regions. Thus, the phenomenon of glial cell migration does not seem to occur synchronously throughout all regions of the brain. As with myelination and gyral complexity, the frontal regions of the brain are the last to fully mature.

A delayed pattern of myelination has been reported in infants with underlying neuroabnormalities (11–13). The presence of peripheral bands in group B infants (score = 2) at an older PMA than the healthy preterm infants in group A may reflect a delay in glial cell migration in babies with neurologic disorders.

Conclusion

We suggest that the bands of low signal intensity seen in the periventricular white matter on T2-weighted MR images are populations of migrating glial cells. Their appearance represents a further marker of normal brain development and should improve evaluation of cerebral maturity in the newborn period.

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