Postnatal encephaloclastic porencephaly—a new lesion?

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Abstract

A previously unrecognised and distinctive pattern of severe brain injury in extreme preterm neonates was observed recently. Fifteen neonates of birth weight 600–1270 g and gestation of 24–32 weeks showed relatively late development on cerebral ultrasound scan of extensive dense and cystic lesions involving the periphery of the brain. The extent of the changes was confirmed at postmortem examination in 11 babies. These changes have been called encephaloclastic porencephaly. The population of babies in whom this has occurred and their clinical outcome has been reviewed, with comparison between the evolution of the ultrasound changes and pathological findings at postmortem examination.

The susceptibility of the brain in the sick premature infant to insult is well recognised, with important consequent morbidity and mortality. Improved techniques in brain ultrasonography have led to early recognition of brain injury, and in particular certain patterns of injury have been well defined in the literature over recent years.[1][2] In the patient who suffers cerebral ischaemia periventricular leucomalacia is characteristic, but in the mature infant subcortical leucomalacia is more typical. Current evidence suggests that the site of the lesion is determined by the development and maturation of the cerebral arterial blood supply.[3–5]

Recently we have observed a new pattern of injury in a series of 15 preterm neonates at Birmingham Maternity Hospital. In these infants we observed the relatively late development of extensive echodense and cystic lesions involving the periphery of the cerebrum. The pattern seen on ultrasonography and confirmed at postmortem examination in two thirds of cases has not previously been reported in liveborn infants, although pathologically it has similarities with the lesion of hydranencephaly in the fetus.[6] The population of neonates is reviewed and the evolution of ultrasound changes and correlation with pathological findings described.

Subjects and methods

The neonatal intensive care unit at Birmingham Maternity Hospital is the regional referral unit for the West Midlands. All neonates admitted to intensive care undergo cerebral ultrasound scanning twice a week and later once a week when the infant is clinically stable. The majority of scans were performed by one experienced observer (PRP). A Hewlett Packard ultrasound imaging system with a 5 mHz phased focused array transducer was used. The anterior fontanelle was used as an acoustic window. The method used and our experience at this unit has been reported previously.[1]

During the study period September 1988 to April 1990, 265 babies of birth weight <1500 g were admitted to our unit. In 15 neonates a new pattern of brain injury was noted. Clinical data were drawn for these 15 neonates from contemporary case notes and the evolution of ultrasound scan appearances analysed.

A postmortem examination was performed by the regional perinatal pathologist (DIR) in 11 of the 14 babies that have died.

Results

(1) CLINICAL DETAILS AND OUTCOME
Clinical details of the neonates under discussion are outlined in table 1. All were sick preterm

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Table 1 Clinical details of the neonates

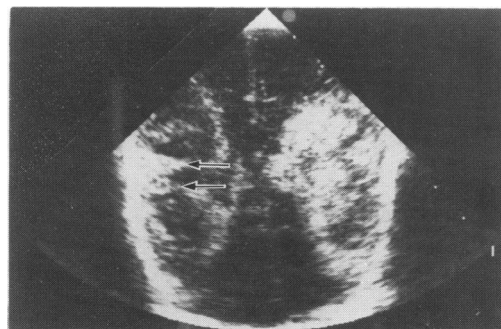| Infant No	Gestation (weeks)	Birth weight (g)	No of days ventilated	No with mean blood pressure <30 mm Hg in first 24 hours	Age at death (days)
1	25	600	27	Yes	27
2	28	1060	9	No	42
3	26	1230	14	Yes	19
4	27	810	14	Yes	31
5	24	630	13	Yes	13
6	26	790	9	No	21
7	26	990	7	No	34
8	27	920	25	Yes	25
9	26	1240	21	Yes	39
10	32	1270	12	No	23
11	26	700	13	No	22
12	29	1260	3	No	Alive
13	27	1110	6	Yes	39
14	28	690	14	No	39
15	28	850	32	No	31

Figure 1 Posterior coronal section showing deep echodense sulci on the left (arrowed).
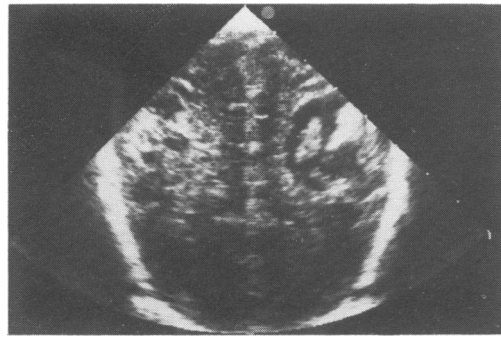
Figure 2   Posterior coronal section showing widespread cystic change in both cerebral hemispheres.
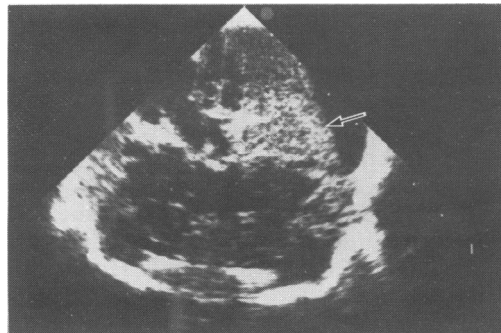

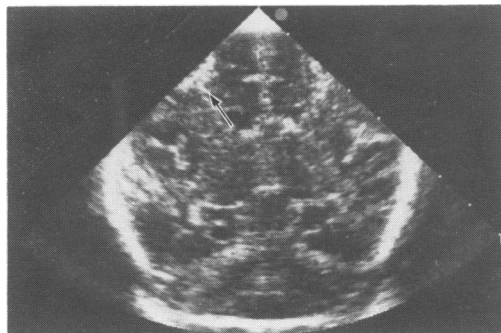Figure 3   Coronal ultrasound showing shrinkage of brain away from skull (arrowed).

Figure 4   Coronal ultrasound scan showing peripheral wedge shaped echodensity on the left (arrowed).

Figure 5   Evolution of ultrasound changes.

neonates whose clinical histories bore all the markers of neonatal intensive care. They were of mean gestation 27 weeks (range 24–32 weeks) and mean birth weight 940 g (range 600–1270 g). Fourteen required ventilation from birth for a mean duration of 15 days. Seven required colloid for the treatment of mean blood pressure <30 mm Hg in the first 24 hours of life but none required inotropic agents. All underwent arterial cannulation. Eleven had a patent ductus arteriosus, seven received indomethacin, and one required surgery.

Outcome was extremely poor with 14 of the 15 neonates dying. All were profoundly abnormal neurologically before they died and eight required treatment for frank convulsions. The one survivor has severe neurological deficit at 12 months.

(2) ULTRASOUND SCAN APPEARANCES

The cerebral ultrasound appearances were characterised by irregular echodense areas extending from the ventricles to the skull margin. They were bilateral, typically affecting the parietal lobes and sparing the medial parts of the hemisphere bordering the longitudinal fissure. Peripherally there were finger like projections, which represent deep echodense sulci, and these together with the medial sparing give a striking characteristic appearance on posterior coronal sections (fig 1).

This appearance was followed by gross cystic changes (fig 2) and sometimes shrinkage of the brain (fig 3). In three cases where evolution of these lesions was observed most closely the earliest changes were cortical wedge shaped densities (fig 4) that progressed rapidly to the
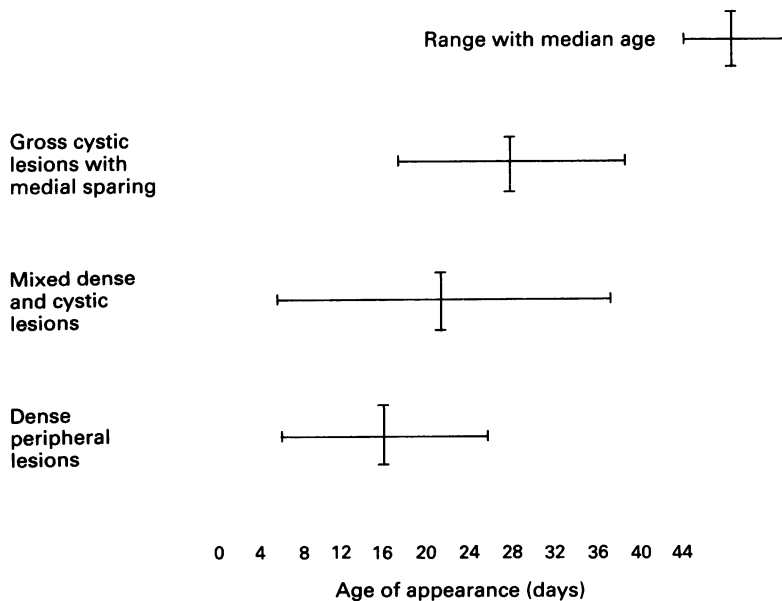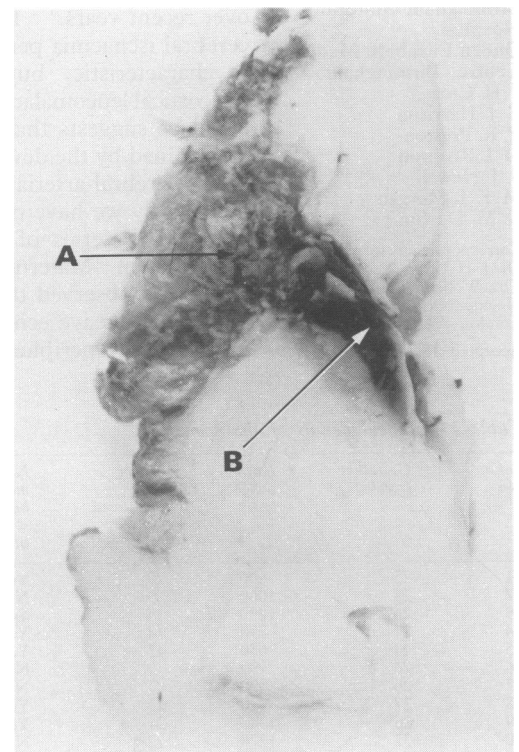

Figure 6   Case 5: coronal section left cerebral hemisphere. Necrotic wedge shaped lesion (A) extending from the cortex to the apex of the lateral ventricle. There is a subependymal haemorrhage in the inferolateral wall of the ventricle (B).

typical mixed cystic and dense lesions. The time of appearance of these changes is shown in fig 5. Other ultrasound abnormalities were present in five babies, namely subependymal haemorrhages alone in three (numbers 4, 9, and 15), a subependymal haemorrhage and periventricular leucomalacia in one (number 7), and a subependymal haemorrhage, intraventricular haemorrhage, and periventricular leucomalacia in another (number 11). In all these five babies these scan appearances were well established and stable at the time when new lesions appeared.

(3) PATHOLOGY (SEE TABLE 2)

The characteristic lesion in the majority of these babies was full thickness necrosis of the cerebral cortex and underlying white matter resulting in communication of the ventricular system with the subarachnoid space (fig 6), which we have termed encephaloclastic porencephaly after the convention of Yakovlev and Wadsworth.[7] Typically the area around the sulcus centralis, sulcus lateralis and insula were involved, although in the more extensive lesions the frontal, parietal, and occipital lobes were affected with relative sparing of the medial surfaces (fig 7). The extent of the lesions varied from relatively narrow clefts to very extensive loss of the superolateral portions of the cerebral hemispheres. In the majority of cases subarachnoid and/or cortical haemorrhages overlay the necrotic lesions (fig 8). Mature lesions typically showed rounded edges to the cortical defects (fig 9) with ragged linings to the deeper surfaces. Microscopy revealed a phagocytic and glial reaction that in many instances was more extensive and
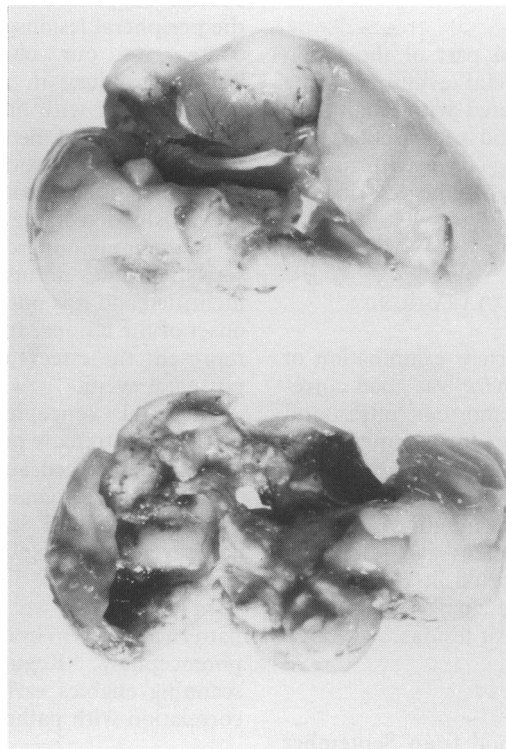

Figure 7 Case 4: cerebral hemispheres viewed from the lateral surfaces. End stage lesions with massive destruction of the cortex and cerebral white matter with preservation of the medial surfaces can be seen.
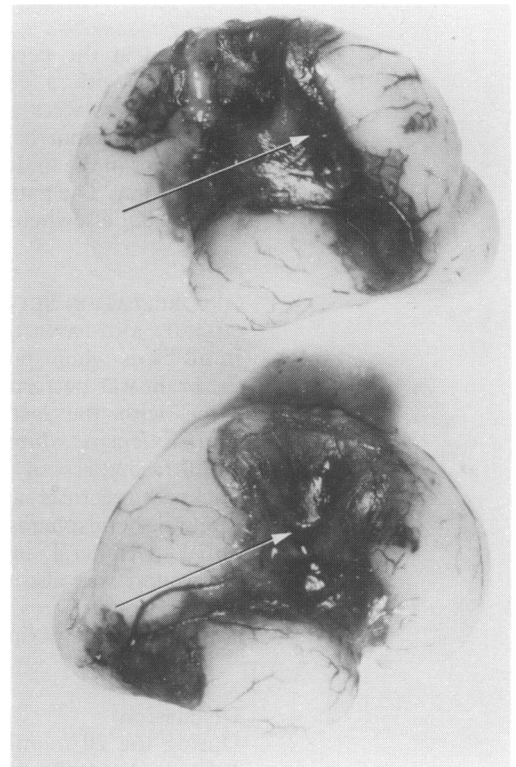

Figure 8 Case 5: lateral surfaces of the cerebral hemispheres. Subarachnoid haemorrhages overlying necrotic lesions have led to collapse of the hemispheres (arrowed).

Table 2 Pathological lesions in cerebral hemispheres by extent and site. Lesions were present in both hemispheres in all cases but differed in degree

Infant No	Subarachnoid or cortical haemorrhage	Cortical necrosis			Site			Other lesions
		Superficial	White matter	Full thickness	Frontal	Temporoparietal	Occipital	
1				No postmortem examination			+	
2	–	–	–	+	+	+	+	
3	+	–	–	+	–	+	+	
4	–	–	–	+	+	+	+	
5	+	+	+	+	–	+	–	
6	+	+	+	+	–	+	+	Old PVL
7	+	–	–	+	–	+	–	Cystic PVL
8				No postmortem examination				
9			Brain disintegrated at postmortem examination					
10				No postmortem examination				
11	+	–	–	+	–	+	+	
12	Alive							
13	+	–	–	+	+	+	+	
14	+	–	+	+	–	+	–	
15	+	–	+	+	+	+	–	

PVL=periventricular leucomalacia.

Figure 9 Case 14: coronal section of the cerebral hemispheres. Older lesions with rounded cortical margins can be seen. The partial thickness lesion has a ragged deep lining (arrowed).

advanced at the peripheral part of the lesion consistent with a centripetal evolution. The earlier lesions were associated with small subarachnoid haemorrhages and perivascular haemorrhages in the underlying cortex with a radial distribution. The pathology will be described in more detail elsewhere.

(4) CORRELATION BETWEEN ULTRASOUND CHANGES AND PATHOLOGY

In all cases where postmortem examination of the brain was performed there was good correlation with the last antemortem ultrasound scan. Extensive white matter involvement seen on ultrasound scan was confirmed with full thickness necrosis and involvement of both cerebral hemispheres seen in all cases. The initial peripheral involvement suggested on ultrasound was also supported at postmortem examination in cases where changes were more advanced to the periphery of lesions.

Discussion

During the 20 month period from September 1988–August 1990 at the Birmingham Maternity Hospital there were 15 neonates who showed a different pattern of severe brain injury to that previously described. Characteristically, these changes appeared late in the neonatal course. They were extensive, bilateral, and involved the periphery of the brain. Pathological findings confirmed ultrasound appearances, with full thickness necrosis of cerebral cortex and white matter. These findings are not in keeping with the classic pattern of brain injury previously described.

Periventricular leucomalacia is well recognised in the preterm infant and occurs in the watershed zones of arterial supply in the deep white matter of the brain.[3–6] [8] [9] Possible variations in white matter injury in these infants has been reported recently[10] but none in the pattern that we have described here. The characteristics of encephaloclastic porencephaly as we have seen are (i) an initial peripheral lesion, (ii) centripetal extension, and (iii) destruction of the cerebral

mantle with relative sparing of the medial structures seen at postmortem, resembling hydranencephaly.[6] Encephaloclastic porencephaly has been previously described as the response of the brain to insult in the second trimester at a time when neuronal migration is complete but before glial reactivity is well developed.[11] Such lesions have been described in term infants who present at birth or soon after when clinical neurological symptoms have been recognised.[12]

Despite the wealth of literature on neonatal cranial ultrasound,[1] [2] [13–16] postnatal encephaloclastic porencephaly has not been previously described. The exact aetiology remains obscure. The neonatal course of the infants described here is typical of any neonate of birth weight <1500 g requiring intensive care, and there is no new procedure or technique that has been used. The presence of extensive necrosis is strongly suggestive of ischaemic injury, although the peripheral lesions are hard to explain in the context of our current understanding of ischaemic injury in the preterm brain. It is possible that with improved techniques and understanding of neonatal intensive care and the subsequent protracted survival of these neonates, early pathological changes not previously detectable on ultrasound scan are now becoming apparent at a later date. In this series of babies no insult to the brain has been identified and it is not possible to time the exact onset of the lesions. It seems probable that they represent the effects of an as yet unidentified postnatal event.

Postnatal encephaloclastic porencephaly carries an extremely poor prognosis. All but one of our infants died and before death eight had evidence of neurological abnormality requiring treatment for frank seizures. The only survivor had severe neurological deficit at follow up at 12 months.

In conclusion we report a new distinctive pattern of preterm brain injury, encephaloclastic porencephaly. Regular cerebral ultrasound scanning enables early recognition, with good correlation with pathological data.

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Meningococcal disease and the flu

The meningococcus is usually a peaceable organism sitting quietly in the nasopharynx and seemingly bearing no grudge. Why then does it become so malign all of a sudden? Variations in virulence may provide some explanation and clearly there are host and environmental factors involved in the propensity for young children. It has been suggested for a long time that upper respiratory virus infections might predispose to meningococcal disease by either facilitating the entry of the bacterium into the tissues and then into the blood or immune suppression.

In the last month of 1989 and the first of 1990 there was an epidemic of influenza A in England and Wales followed by an increase in meningococcal disease as judged by the number of isolates submitted to the Meningococcal Reference Laboratory. Data presented in the *Lancet* (Keith AV Cartwright and colleagues, 1991;338:554–7) showed that the interval between the two epidemics was about two weeks. Similarly timed increases in meningococcal disease also followed influenza epidemics in 1976 and 1957. The *Lancet* paper presents other less convincing data in addition to the epidemiological findings. A serum antibody titre to influenza A/England of 80 or more was found in 18·5% of 54 normal schoolchildren before the influenza epidemic, in 9% of control sera taken during or after the epidemic, in 28% of 43 patients convalescing from meningococcal disease, and in 91% of 23 people convalescing from influenza. The authors conclude that these serological data support an association between meningococcal disease and recent influenza (odds ratio about 4) but the twofold difference in positive rates in the two populations of control sera to my mind casts doubt on the validity of the conclusion. If 18% can by chance become 9% it can presumably by the same chance become 28%. A simultaneous questionnaire study of the incidence of influenzal symptoms before the meningococcal outbreak in cases and controls gave equivocal results and had little scientific validity.

It seems, therefore, that there is epidemiological evidence from three different years that an influenza epidemic may be followed two weeks later by an increase in meningococcal disease. The risk is very small, however; the authors estimate that 100 000 cases of influenza might give rise to one case of meningococcal disease. On that basis it would be necessary to immunise a million people against influenza to prevent a single case of postinfluenzal meningococcal disease (assuming that the influenza would affected one in 10 of the population) and no changes to current immunisation policy are recommended as a result of this work.

The subjects of the serological study were all over 10 years old and the significance of influenza for meningococcal disease in young children is uncertain. Meningococci sent to the Meningococcal Reference Laboratory after the influenza epidemic were less commonly from children under the age of 10 than usual, suggesting that any predisposing effect of influenza may be less common in younger children. The work is of theoretical interest but it seems to offer no obvious insights as regards the prevention of meningococcal disease in children.

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