

Pachygyria in a neonate with trisomy 21

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Pachygyria is a neuronal migration disorder characterized by reduced and broad cerebral gyri.¹ The regions of the brain with pachygyria have an abnormally thick cortex that lacks normal folding and has deficient layering. The role of inheritance has been speculated in its causation, but no definite genetic locus has been identified.^{2,3} The clinical manifestations of pachygyria range from marked hypotonia to frank seizure. Several etiological factors have been described, including cytomegalovirus infection, prenatal cocaine exposure, metabolic disorder and syndromic forms.⁴⁻⁹ However, an extensive literature search showed no previous report on an association of pachygyria with Down syndrome/trisomy 21.

CASE

The baby boy was the second of twins, delivered by cesarean section secondary to breech presentation. The first twin was delivered vaginally. The gestational age was 28^{5/7} weeks. The mother was a 19-year-old woman, gravida 3, para 0111. Antenatal ultrasonography confirmed the twin gestation with anterior placentas and two sacs (dizygotic, dichorionic). The serology for hepatitis, syphilis and HIV were negative. She was rubella immune and denied use of any illicit drugs. She was tocolyzed with magnesium sulfate. Two doses of betamethasones were given and she also received erythromycin and ampicillin prior to delivery. The labor was uneventful. The baby cried soon after birth. The Apgar score was 7 and 9 at one and five minutes, respectively. Birth weight was 1315 grams, length was 35 cm and head circumference was 28 cm, all appropriate for gestational age.

Physical examination showed a hypotonic baby with upslanting eyes, simian creases and flat facies. The chest was clear with a soft systolic murmur. The abdomen was soft and no other deformity was noted. Initial investigation showed normal blood cell counts and electrolytes. Further investigations, including the cytogenetic studies, showed a karyotype of 47, XY, + 21. The echocardiogram revealed small patent ductus arteriosus and the renal ultrasound was normal. On day 38 of life (sixth

week chronological age or 35 weeks postmenstrual age /corrected age) some athetoid movements were noted in addition to the previously observed hypotonia. After neurology consultation, a magnetic resonance imaging (MRI) was obtained that showed generalized pachygyria with no evidence of a basal ganglia lesion or midline defects (Figures 1-3). The electroencephalogram (EEG) showed low voltage activity of 2-3 Hz with no epileptic activity.

The baby remained on minimal supplemental oxygen until day 26 of life and was then weaned to room air. The baby was stable on mostly oral feeding and gaining weight. The head circumference was 32 cm. The eye examination showed a mature retina and the baby passed the hearing test.

DISCUSSION

The MRI of a premature neonate reflects their stage of CNS development.¹⁰ An MRI obtained at 24 weeks

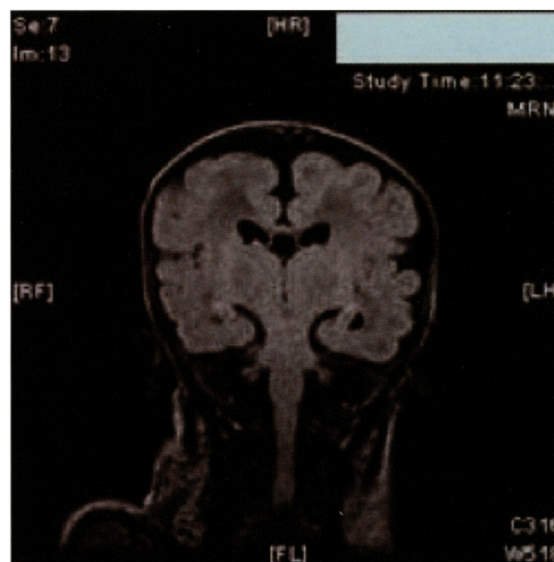


Figure 1. MRI of the brain, coronal image.

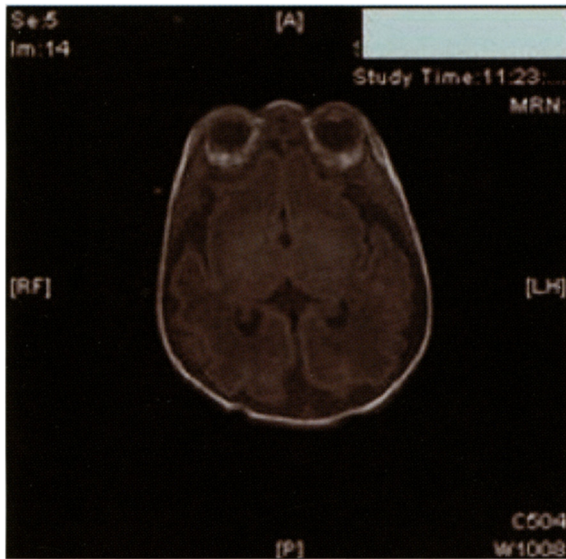


Figure 2. MRI brain, axial image.

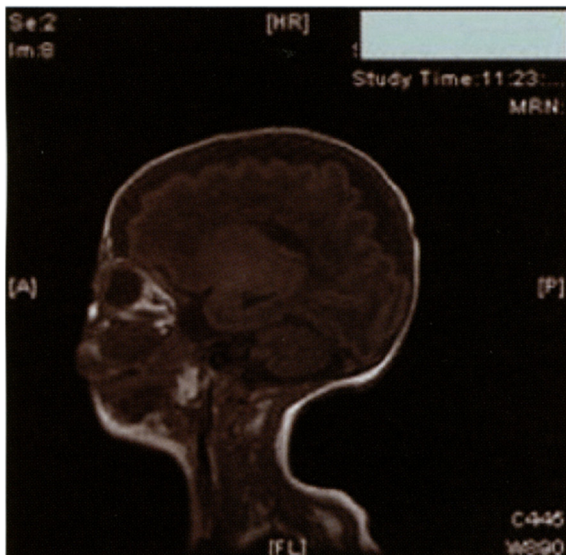


Figure 3. MRI brain, sagittal image.

will be similar for that of a lissencephalic full-term infant and that of a 28-32 week premature neonate will look like a full term with pachygyria. Thus, it could be arguable that the pachygyria observed in the case could just be due to the prematurity. In fact, the MRI in the case was done at the postnatal age of 38 days (at about 35 weeks postmenstrual age) suggesting that pachygyria may not be just a reflection of a very premature brain.

The brains of children with Down syndrome have been shown to be of smaller volume, but no definite neuronal defect was found.¹² The exact etiology for the neurological involvement including hypotonia and mental retardation associated with Down syndrome remains a mystery. Thus it will be interesting to find out if the association observed is coincidental or there is some common underlying genetic basis. Although the case presented above was a twin exposed to same prenatal and maternal conditions, a completely different genetic makeup may explain the dizygosity with occurrence of the trisomy 21 in one. We did not perform the brain MRI on the other twin, as by the time we discovered pachygyria he was discharged from the hospital.

The exact pathology for hypotonia and neurological symptoms in a patient with Down syndrome is not well understood and these symptoms usually never get investigated as compared to central nervous system symptoms noted otherwise. Thus, this case report might be used as an example in looking further into the CNS lesions and structural pathology in Down syndrome. MRI of brain has been described as an excellent diagnostic tool for brain pathology.¹¹ Thus, in light of the association observed in our case, we recommend routine use of MRI of the brain in all Down syndrome neonates so that more can be known about the association between structural brain lesions and the CNS symptomatology frequently observed in infants with trisomy 21. In addition, cytogenetic studies should be done to look at the genetic basis of this interesting observation.

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