PINA bifida occulta is a congenital dorsal spinal dysraphism with intact skin overlying a wide spectrum of different possible abnormalities of the midline. It is considered a sporadic event, but familial recurrence of SBO in siblings has been described. This is the first English language report on the occurrence of 2 different types of SBO in monozygotic twins.

**Case Report**

Two monozygotic female twins were born at term by ventouse delivery after an uncomplicated gestation during which they shared the placenta although they had 2 separated sacs. Monozygosity was determined at birth on the basis of a genetic consultation. The results of fetal ultrasound scans were reported as normal, and the mother’s diet had been supplemented with folic acid during pregnancy. When the twins were examined at birth, no pathological findings were identified on Twin 1, while Twin 2 was found to have a 3–4 cm soft swelling over the lumbosacral region with normal results of neurological examination in her lower limbs. Ultrasonographic examination of the spine and MR imaging confirmed the clinical diagnosis of LMMC (Fig. 1). Sphincter functions and the results of a renal ultrasound scan were normal. The patient was treated conservatively.

When the twins were 9 months old, Twin 2’s neurological development started to be delayed compared with that of her sister. Twin 1 began to perform stepping movements and to crawl, but Twin 2 did not. Twin 2 also became quite distressed by any pressure on the lesion and was unable to lie on her back. She underwent surgical untethering of the spinal cord and partial excision of the lipoma when she was 11 months old. The lipoma was dissected circumferentially until the conus medullaris was reached, where it was not possible to identify an anatomical plane of dissection. The dura mater was opened, and a thick tethered filum was untethered, reducing the traction on the conus medullaris.

When the twins were 2 1/2 years old a small dimple suggestive of a dermal sinus tract was noted at the lower lumbar spine of Twin 1, the previously unaffected sister; it was closed and no discharge was ever noticed through it. Twin 1 was otherwise developing well. A spine MR imaging study revealed a tethered cord (Fig. 2).

When Twin 1 was 3 years old she underwent untethering of the spinal cord. At surgery the terminal filum was thickened and exerted some traction on the conus medullaris that reduced after the filum was released.

At last follow-up the twins were 6 years old. Twin 1’s neurological and urological functions were completely normal; Twin 2, who had previously shown a complete recovery to a normal level of neurological development, presented with a reduction of power in her legs. An MR imaging study revealed retethering of the spinal cord in Twin 2. Surgical treatment was offered, but the child’s parents decided to wait.

**Discussion**

Neural tube defects are a group of congenital malformations of brain and spine which affect an average of 1 per 1000 pregnancies. They are caused by a maldevelopment of the neural tube during the process called neurulation (between the 18th and 28th days of gestation). During
Spina bifida in monozygotic twins

primary neurulation the primary neural tube forms and becomes covered by surface ectoderm. This structure will differentiate into the brain and most of the spinal cord. A failure at this stage produces open defects like myelomeningocele. During secondary neurulation the mesenchymal cells still present at the end of this structure undergo condensation and epithelialization to form a secondary neural tube that is continuous with the primary neural tube and will differentiate into the lowest portion of the spinal cord. A failure at this stage can produce closed defects, also described as spina bifida occulta (SBO), a term that refers to a wide spectrum of congenital anomalies including LMMC and fatty filum. The incidence of SBO is not known, because symptoms can have a late onset, even in adult life, but it is estimated as 1 in 4000 births, with LMMC accounting for 20–50% of the cases.

The etiology of NTDs is still debated, and they are considered multifactorial malformations depending on both genetic and environmental factors. So far, it is not known which genes are involved in the neurulation process, nor is it clear whether primary and secondary neurulation depend on the same group of genes or on 2 or more different groups.

Many studies on mice have ruled out specific mutations...
and/or deletions of specific genes as a cause of NTDs, but when the DNA of patients with NTDs has been examined for the equivalent genes, there have been only a few cases with mildly significant findings. When the parents’ DNA was studied also, no variations were found to be passed from parent to child with the positively transmitted allele.8,15,18–20

The role of environmental factors is confirmed by the effectiveness of dietary folic acid supplementation before and during pregnancy in preventing open defects.4 Nevertheless, McNeely and Howes12 report that this supplementation does not reduce the number of closed defects, suggesting that primary and secondary neurulation could be independent processes from a genetic point of view.

Neural tube defects have been and are still considered as sporadic events because usually only one individual is affected in a family. It is remarkable that from population-based studies and birth defects registries the recurrence risk for NTDs in siblings of patients with LMMC is 2–5% with no recurrence of LMMC.5,6,9,16 The rare event of recurrence of LMMC in the same family was reported only twice previously, and it suggests a Mendelian inheritance (autosomal recessive or autosomal dominant with somatic mosaicism).10,17

The presence of SBO in the twins we report on is a rare feature of this form that can be described as familial NTDs. It is interesting to note at least 2 facts: 1) The twins were monozygotic and the defect was closed in both, but Twin 2 presented at birth with an LMMC whereas Twin 1 was affected by a tethered cord that was suspected only 2 years after birth. 2) The mother received folic acid supplementation during pregnancy.

It is well described that monozygotic twins can be affected differently by genetic syndromes or by pathological conditions that have a multifactorial etiology. Epidemiological studies have ruled out that the process of twinning itself may be associated with a higher risk for NTDs.7,21,22 Moreover, prenatal diagnosis of LMMC and other manifestations of SBO can be difficult. These conditions are not easy to detect with ultrasonography, even when performed by an expert; they are not usually associated with malformation of the brain and no evidence of the conditions is present in maternal serum or amniotic fluid.1–3,11,13

Conclusions

Due to the lack of knowledge concerning the genetic basis of neurulation, the risk of recurrence of NTDs is difficult to predict. As reported above, for the sporadic form it is between 2 and 5%,5,6,9,16 but when a familial form is suspected the risk of NTD recurrence in siblings rises to 25%.10 Therefore we think that at birth monozygotic twins should be carefully examined clinically to rule out any abnormalities including small cutaneous stigmata, and a lower threshold for neuroradiological investigations could be accepted when a defect like NTD is found in a single twin.

Disclaimer

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

3. Chreston J, Sherman SJ: Sonographic detection of lipomyelome-
ningocoele: a retrospective documentation. J Clin Ultrasound 25:
50–51, 1997
4. Copp AJ, Greene ND, Murdoch NJ: The genetic basis of mam-
5. Forrester MB, Merz RD: Precurcence risk of neural tube defects in siblings of infants with lipomyelomeningocele. Genet Med 7:
457, 2005
6. Frey G, Hauser WA: Epidemiology of neural tube defects. Epi-
lepsia 44 (3 Suppl):4–13, 2003
1053, 1994
8. Joosten PH, Tjoepel M, Mariman EC, Van Zoelen EJ: Promoter haplotype combinations of the platelet-derived growth factor a-
receptor gene predispose to human neural tube defects. Nat Ge-
AK, et al: International study of sex ratio and twinning of neural
tube defects. Teratology 50:322–331, 1994
10. Kannu P, Furneaux C, Altimos S: Familial lipomyelomeningo-
11. Kim SY, McGahan JP, Bogdan JE, McGrew W: Prenatal diagno-
sis of lipomyelomeningocele. J Ultrasound Med 19:801–805,
2000
12. McNeely PD, Howes WJ: Ineffectiveness of dietary folate acid sup-
plementation on the incidence of lipomyelomeningocele: patho-
100, 2004
Ciba Found Symp 181:70–89, 1994
15. Rogner UC, Danoy P, Matsuda F, Moore GE, Stanier P, Avner P:
SNPs in the Cpg island of NAPIL2: a possible link between DNA methylation and neural tube defects? Am J Med Genet
110:208–214, 2002
16. Sebold CD, Melvin EC, Siegel D, Mehltretter L, Enterline DS, Nye
JS, et al: Recurrence risks for neural tube defects in siblings of
patients with lipomyelomeningocele. Genet Med 7:64–67, 2005
17. Seeds JW, Power SK: Early prenatal diagnosis of familial lipo-
18. Speer MC, Melvin EC, Viles RD, Bauer KA, Rampersaud E,
Drake C, et al: T locus shows no evidence for linkage disequilibri-
um or mutation in American Caucasian neural tube defect fam-
19. Volcik KA, Blanton SH, Kruzel MC, Townsend IT, Tyerman
GH, Mier RJ, et al: Testing for genetic associations with the PAX
20. Volcik KA, Blanton SH, Kruzel MC, Townsend IT, Tyerman
GH, Mier RJ, et al: Testing for genetic associations with the PAX
gene family in a spina bifida population. Am J Med Genet 110:
195–202, 2002
21. Windham GC, Bjerkedal T: Malformations in twins and their sib-
87–95, 1984

Address correspondence to: Neil Buxton, F.R.C.S.(NS), Department of Neurosurgery–Littlewoods Neuroscience Unit, Royal Liverpool Children’s Hospital NHS Trust, Eaton Road, L12 2AP, Liverpool, United Kingdom. email: neilbuxton@doctors.org.uk.