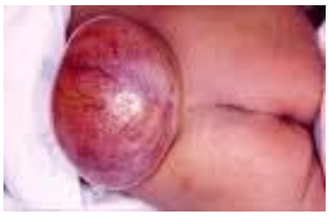
CASE FIVE

Short case number: 3_12_05
Category: Children & Young People
Discipline: Paediatrics Surgery
Setting: Hospital Ward
Topic: Neural tube defects_myelomeningocoele

Case



You are the intern on the paediatric surgical team. Jack Landers is 12 hours old, he has been transferred to the newborn high dependency unit, following his delivery by LSCS. Jack has a myelomeningocoele which was detected on antenatal ultrasound performed at 35 weeks because his mother had noticed reduced foetal movement.

Questions

1. Before the team go to assess Jack, the neurosurgical registrar asks you to refresh his memory about the embryology and anatomy of the spinal cord and vertebrae and asks you to explain the abnormalities that occur in spina bifida and myelomeningocoele.
2. Briefly outline the classification of neural tube defects.
3. The team meet with Jack's parents and outline the management of Jack's problem. Explain the key aspects of the management of myelomeningocoele, taking into account the specific problems in the newborn.
4. The management of neural tube defects requires a multidisciplinary approach, detail the ongoing management issues for children and families and the relevant members of the management team.
5. Outline the recommendations regarding the use of folate in the prevention of neural tube defects. What recommendations would be given to Jack's mother for future pregnancies?

Suggested reading:

- South M, Isaacs D editors. Practical Paediatrics. 7th edition. Edinburgh: Churchill Livingstone; 2012.
- Neuroembryology: Neural Tube Development: Formation and Closure
  Pathophysiology and clinical manifestations of myelomeningocele (spina bifida)

ANSWERS

1. The primitive streak is a linear thickening on the dorsal surface of the epiblast in which cells of the epiblast form endoderm and mesoderm. The dorsal ectodermal surface of the early embryo thickens and elongates to form the neural plate. By the 20th day post fertilization the neural plate becomes the neural groove. Rapid cell proliferation at the margins of the neural plate alter its configuration so that a midline neural groove forms between neural folds, which gradually deepens. The anterior end of the neural plate enlarges and will form the brain while the caudal portion of the neural plate will form the spinal cord. The cavity of the developing neural tube is destined to become the ventricular system. Ectoderm at the margins of the neural folds represent cells destined to become neural crest cells that will give rise to the main elements of the peripheral nervous system.

   The lateral edges of the neural folds grow medially and unite in the midline to form the neural tube which then separates from the ectoderm. Fusion begins in the cervical region on the 21st day and proceeds in both directions until the neural plate becomes the neural tube. Cells from the margins of the neural tube detach from the ectodermal neural folds to form clusters of neural crest cells. These dorsally located cells migrate peripherally to become sensory ganglia of the cranial and spinal nerves, autonomic and enteric ganglia, Schwann cells, melanocytes, adrenal chromaffin cells, and the pia/arachnoid membranes.

   By about 25 days the cephalic and caudal closure of the neural tube, at the anterior neuropore and posterior neuropore, becomes complete and the neural plate is converted into the neural tube. After closure of the neural tube, the expanded rostral portion of the neural tube will differentiate and subdivide into three vesicles representing the forebrain, midbrain and hindbrain.

   The term neural tube defect (NTD) refers to a group of malformations involving the brain and/or spinal cord in association with varying degrees of absence or malformation of the overlying tissues: meninges, bone, muscle and skin.

   Myelomeningocoele involves all the tissue layers including the skin and bone and is an outpouching of the spinal cord through the posterior bony vertebral column that has failed to form. The term *spina bifida* refers to the normal bony projection over the spine being divided or 'bifid' and can be divided into *spina bifida occulta* and *spina bifida cystica*.

2. **Classification of neural tube defects**

   Anencephaly
   - At birth, presents as an opened, malformed skull and brain.
   - Most babies are stillborn
   - No effective treatment is possible
   - Death usually occurs within hours or days

   Cranium bifidum

   Cranial meningocoele
   - The underlying brain is normal
   - A meningeal sac protrudes through a skull defect

   Encephalocoele
   - A midline sac protrudes that may contain brain
   - Hydrocephalus is common

   Spina bifida occulta
   - One or more vertebral arches are incomplete posteriorly but the overlying skin is intact
   - Diagnosed incidentally, e.g. as the result of an X-ray of the spinal column during other investigations **. Occurs in 5% of live births**
   - Spinal cord usually normal, however, a number of abnormalities of the spinal cord have been

described
- Ectodermal abnormalities may be associated
  - a dermal pit
  - a depression with a tuft of hair
    Capillary haemangioma
  - a fatty swelling
- The ectodermal component
  - may communicate with the dura
  - may pose some risk of intraspinal infection (if associated with a dural sinus)

The ectodermal component, if present, warrants full neurological examination and possibly Ultrasound scan or MRI of the spinal cord

Lipomeningocoele

Occurs when excessive lipomatous tissue is within or attached to the spinal cord or filum terminale. This group of malformations are by far the most common form of neural tube defect and vary from an enlarged filum terminale to a huge fatty mass occupying much of the dorsal lumbosacral region.

In this instance, the cord may be tethered to the wall of the spinal column and require detethering as the child grows to prevent 'stretching' of the cord which may have permanent neurological effects

Spina bifida cystica

Myelomeningocoele, in which vertebral column, skin, meninges and spinal cord are involved. CSF, meninges and spinal cord protrude into an external sac
(Meningocoele, same as above except the spinal cord is not involved) • Almost always obvious at birth (most frequently, a midline sac protrudes through a spinal defect)
Amount of skin covering the lesion is variable

- May occur anywhere along the length of the spinal column
- The lumbar and lumbosacral regions are the most frequent anatomical levels
- Abnormal spinal cord tissue and nerve roots may be readily apparent macroscopically
- There may be spinal abnormalities such as kyphosis at the site of the lesion
- Functional deficits include:
  - varying degrees of paraplegia, with motor and sensory impairment
  - Arnold-Chairi Type II malformation and approximately 80% of children with lesion develop hydrocephalus
  - 80% of people with spina bifida have normal IQ, but many have problems with more subtle executive cognitive problems
  - neuropathic sphincter dysfunction
    Severe constipation

Sacral agenesis

Diastematomyelia - spinal cord is split into two hemicords with each having a set of dorsal and ventral nerve roots

3. A team approach that includes the parents is essential for the proper management of myelomeningocoele. An important factor, which compounds the disability, is that the defect is apparent at birth. Information given to the parents and the manner in which it is conveyed will influence their reaction at this most vulnerable time and will affect the future of the child and the family. Medical specialists in this team include the neurosurgeon, orthopaedic surgeon and urologist. The medical team leader is most appropriately a paediatrician or paediatric rehabilitation specialist with special skills in the field of child development and rehabilitation.

The medical team leader will coordinate care but, importantly, will also manage and advise on the multiple problems experienced by the children and their families.
It is possible to predict with considerable accuracy the potential for future impairment in a number of areas. These include ambulation and subsequent mobility, probable bowel and bladder function, and hydrocephalus, with its probable sequelae. It is much more difficult to predict the effects that these impairments will have on the lifestyle of the individual and family. Also, it is possible to recognize early those lesions that are inoperable because of massive bony deformity and extensive skin loss, which would prevent closure of the defect.

The specific problems are as follows:

Children with high lesions (thoracic and thoracolumbar), hydrocephalus at birth, major kyphosis or other significant problems have a significantly increased mortality in early life and substantial morbidity if they survive. In these circumstances, in discussion with the family, supportive care only may be recommended. If the infant survives the perinatal period, elective surgical care may be indicated with early repair/removal of the lesion usually recommended.
Careful serial evaluation of head circumference and ventricular size by ultrasound or CT scan will indicate if hydrocephalus is developing, if so a shunt procedure is recommended. Baseline orthopaedic, urology and neurosurgery assessments provide the basis for ongoing discussions with the family and management of the condition.

Babies born with a myelomeningocoele are often prophylactically put onto a clean intermittent catheterisation programme in order to protect the kidneys at or shortly after birth. It is critical to begin to establish an empathetic, therapeutic relationships with the parents in the newborn period that forms the foundation for ongoing support throughout childhood.

4. Ongoing management problems include disability issues, school integration, interventions to improve functional outcome and various activities to support the parents and child through the many problems, both physical and psychological, that invariably arise. The physiotherapist, occupational therapist, orthotist, psychologist and medical social worker, together with trained hospital and community-based nursing staff and teachers, are important members of the team.
The team has three major goals:
   - to promote good health in the short and long term
   - to promote maximum function in the child so that, as nearly as possible, normal developmental sequences and timing can be followed to enable maximal independence for the child and family
   - to promote good family functioning

Ongoing management issues include the following:
- <u>management of physical disability and mobility</u>: physiotherapists play an essential role in reducing deformities and encouraging mobility. Splinting, casting and passive stretching in early life are the mainstays of treatment of foot deformities, common at birth. Surgery may be necessary for persistent foot deformities or dislocated hips if the child is likely to walk. The outlook for walking depends on the level of the spinal cord lesion and motivation.

- <u>spinal deformities</u>: a significant percentage of children will develop scoliosis and many of these will require spinal instrumentation
- <u>neuropathic fracture</u>: fractures of the lower limbs, due to osteopenia, are common in children with myelomeningocoele. Fractures may occur with minimal trauma.
Encouraging children to walk or stand, nutrition, calcium and vitamin D may all be important factors in management.

- sensory deficit and skin care: pressure ulcers or burns in anaesthetic areas are common. Early recognition and treatment is essential to prevent long periods of morbidity and hospitalization.
- neuropathic bladder: almost all children with myelomeningocoele have a neuropathic bladder. Failure to empty the bladder may lead to recurrent urinary tract infections, vesicoureteric reflux, renal calculi and hydronephrosis.

Management is by clean, intermittent catheterization performed 4 – 5 times daily.
Prophylactic antibiotics may be required for recurrent urinary infections and regular assessment of renal function is essential throughout the person's life. This is crucial as 25% of people with spina bifida die of end stage renal disease.

- neuropathic bowel: most children have limited or absent rectal sensation and may have little or no bowel control. Constipation with megacolon, faecal impaction and overflow incontinence is the major risk in spina bifida. Refractory cases may require regular bowel washouts and a surgical procedure such as a caecostomy.

- sexual function: many people with spina bifida achieve satisfactory sexual relationships. In females, pregnancy has been achieved in many individuals and is generally a positive experience however urinary tract infections, worsening pressure sores and spinal problems are particularly common. In males, difficulties range from impotence to retrograde ejaculation and infertility. Sexual counseling is important in adolescence.

- tethered spinal cord: following repair of a myelomengingocoele, the lower end of spinal cord may become tethered to the site of repair. As the child grows, this may cause progressive neurological deterioration in motor or sensory function, or in bladder control. MRI scans are performed to demonstrate the tethering process. With significant deterioration, neurosurgical release of the tethered cord may be necessary.

- Arnold-Chiari malformation: is present in a significant number of children with myelomeningocoele and is elegantly demonstrated by MRI. Life-threatening episodes may necessitate neurosurgical intervention to decompress the posterior fossa.

- education: children with myelomeningocoele often have specific learning problems, requiring assistance at school. Overall intelligence is generally in the low average range, verbal IQ is usually considerably higher than performance IQ.

Many have deceptively good expressive language but with a paucity of meaning and content of speech. Difficulties with mathematical concepts are very common, as are problems with abstract reasoning. Many children have a poor attention span, with distractibility and problems with organisation. They also have a lack of persistence and lack of time-management skills. Problems with fine motor control and visual perceptual difficulties are frequently present. Most children with spina bifida attend normal schools with varying levels of assistance.

- social and emotional adjustment and transition to adulthood: a child with a chronic disability places severe strains on the emotional and financial resources of a family. During the teenage years, the usual problems of adolescence are superimposed on the difficulties associated with the disability, and these young people need sensitive counselling. For the families, parent groups provide valuable practical and emotional support. Young people wish to be independent and break away from what they perceive as overprotection by the medical fraternity however, problems continue to occur, particularly pressure ulcers, shunt and urinary complications.

5. Research has suggested a relationship between maternal diet and the birth of an infant affected by neural tube defects. Medical evidence has confirmed that folic acid (a water-soluble vitamin found in

many fruits, leafy green vegetables, wholegrain breads, cereals and legumes) may prevent the majority of these defects.

Randomized controlled trials and research in a number of countries have demonstrated that supplements containing folic acid are effective in reducing the occurrence of neural tube defects. The protective effect of folate during pregnancy goes beyond NTDs. Supplementation with folic acid has been shown to reduce the risk of congenital heart disease, cleft lip, limb defects, and urinary tract anomalies.

The mechanisms and reasons why folic acid prevents birth defects is unknown however it is hypothesized that the insulin-like growth factor2 gene is differentially methylated and these changes in IGF2 result in improved intrauterine growth and development.

The National Health and Medical Research Council of Australia has recommended the following:

• *all women planning a pregnancy or likely to become pregnant* should be offered advice about folate in the diet and encouraged to increase their folate intake
particularly in the month before and in the first 3 months of pregnancy.

• *Women with a close family history of neural tube defects*(e.g. they or their partner has spina bifida, they have already had an affected child, they have a sibling or
other close relative with a neural tube defect) such as Jack's mother :

• should be referred for genetic counselling

• should be advised to take periconceptual folic acid supplementation 5mg daily.

• should continue to be offered prenatal diagnosis with alpha-foetoprotein estimation and expert ultrasound, by an operator experienced in anatomical scans, at 16 – 18 weeks gestation. There is a residual risk of about 1% in women taking folate supplements who have had a previously affected infant.

Because of the increased risk of neural tube defects in the offspring of women taking some anticonvulsants (notably sodium valproate), these women also should be counselled and offered prenatal diagnosis.