

REVIEW

Postnatal management and outcome for neural tube defects including spina bifida and encephalocoeles

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The incidence of neural tube defects (NTDs) has declined in recent decades, however myelomeningocele and encephalocoele still represent one of the commoner prenatally diagnosed congenital malformations. Improved perinatal and post natal care mean that the mortality associated with these conditions has also fallen. Advances in the multidisciplinary management of children with myelomeningocele have led to significant improvements in functional outcome for many with this condition. However, there remains a substantial population of patients born with NTDs whose life expectancy is substantially reduced and who suffer significant cognitive and physical disability remaining wholly or partially dependant on the care of others into adult life.

This article aims to outline the contemporary early management of these conditions and examine the prospects for functional outcome where possible, attempting to show how early anatomical features of these conditions can help predict where, along the wide spectrum of outcome, a given individual may lie. Copyright © 2009 John Wiley & Sons, Ltd.

KEY WORDS: myelomeningocele; spina bifida aperta; encephalocoele; hydrocephalus

INTRODUCTION

The yearly prevalence of neural tube defects (NTDs) in the UK and Ireland is between 10 and 15 per 10000 births (Busby *et al.*, 2005a). In the European Union approximately 4500 pregnancies per year are affected by these defects (encephalocoele, anencephaly and myelomeningocele). The role of folic acid in the prevention of neural tube defects has been established since the early 1990s (MRC Vitamin Study Research Group, 1991). It is estimated that with adequate pre-conceptual folate supplementation 70% of neural tube defects could be avoided. Whilst current prevalence rates have indeed fallen, this trend was well established prior to the introduction of folate recommendations. Unfortunately, poor education regarding folate supplementation and the high rate of unplanned pregnancy has meant that the full potential of this preventative strategy has not been realized (Busby *et al.*, 2005b).

With improved perinatal, neonatal and neurosurgical care the early mortality associated with neural tube defects has reduced and with active intervention, the majority of children born with these defects will survive. For many, survival will come at the cost of medical problems that require expertise across many disciplines. The emphasis is now on optimizing functional outcome for these children through provision of coordinated multidisciplinary care throughout childhood and beyond. An understanding of the contemporary management of

these conditions and the likely long term prognosis is essential to aid parents in their decision to proceed or not with the pregnancy. It must be emphasized that this review deals exclusively with 'open' neural tube defects. This data cannot be extrapolated to the skin covered, or closed dysraphic states such as lipomyelomeningocele and split cord malformations, who do not have the associated cerebral anomalies and in whom functional prognosis is considerably better.

MANAGEMENT

Perinatal management: mode of delivery

There has been debate about the relative merits of cesarean section versus vaginal delivery for infants known to have open neural tube defects. Does a vaginal delivery increase the risk of infection or damage to the exposed neural tissue? Whilst there are no studies addressing this question for encephalocoele, it would seem not unreasonable to extrapolate what information there is for myelomeningocele to this population as well.

In a prospective, though non randomized study, Luthy found that labor was associated with an increased risk of additional deficit and concluded that delivery by cesarean section before the onset of labor may result in better motor function than vaginal delivery or cesarean section after a period of labor (Luthy *et al.*, 1991). Cesarean section remains the more common mode of delivery, and from a practical standpoint facilitates early liaison with the neurosurgical team regarding transfer and the timing of surgical intervention. There are, however, a number of other well conducted studies that have

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drawn the contrary conclusion. Bensen *et al.* (Bensen *et al.*, 1988) reported an incidence of neonatal meningitis of 6% for children born with myelomeningocele; this incidence was no different between those born by cesarean section and those by vaginal delivery. In this study, outcome as assessed by neurological level was also not influenced by mode of delivery, a finding that has been observed by others (Cochrane *et al.*, 1991; Lewis *et al.*, 2004; Merrill *et al.*, 1998). In summary, there is no clear evidence from the neurosurgical perspective to favor cesarean section in the absence of gross hydrocephalus, breech presentation or other usual obstetric indications.

Presurgical management

The exposed placode should be covered with a sterile dressing in an attempt to avoid contamination and prevent additional damage through excoriation or desiccation. Whilst it is standard practice to administer prophylactic antibiotics again there is little evidence to support this practice so long as surgical closure of the defect is likely to occur within 48–72 h. Microbiological swabs are taken at the time of closure; standard neurosurgical prophylaxis is then given to cover the procedure but not continued unless there is a clear clinical or microbiological reason to do so.

Once considered a neurosurgical emergency there is little evidence to support this and stabilization of the infant is paramount and time should be given for maternal contact.

MYELOMENINGOCELE

In 1972, John Lorber published a controversial paper describing the outcome of a cohort of children born with myelomeningocele (Lorber, 1972). The prognosis was indeed bleak for a significant proportion of those children. His controversial conclusion was that there were at the time of birth a number of clinical features that were deemed to be of such poor prognostic significance that patients fulfilling the 'Lorber criteria' should not be offered active treatment. Instead efforts should be directed to those most likely to benefit in the long term. Over the subsequent 30 years the incidence of myelomeningocele has fallen and so current generations of paediatricians will thus encounter this condition less commonly and their perceptions of prognosis likely to reflect the pessimism of their predecessors. Has the outlook changed for the child born with myelomeningocele in the new millennium? What prospects—functional, cognitive and sociological can be offered to the parents at the time of prenatal counseling?

What follows is an attempt to summarize the contemporary management of the neonate with myelomeningocele and some indication of the likely prognosis given optimal multidisciplinary input.

In utero surgery

On the basis that the neural placode appears to suffer additional damage during the latter part of pregnancy due to the effects of pressure, local trauma and exposure to amniotic fluid, it has been postulated that prenatal repair might improve neurological outcome. At least in the short term motor function has been reported to be better than the predicted for spinal level (Johnson *et al.*, 2003) and the incidence of shunt dependent hydrocephalus is reportedly less, 54% for *in utero* repair compared with 86% for historical controls (Tulipan *et al.*, 2003). The morbidity, for both mother and child is however not insignificant and the real long term benefit not confirmed. A randomized trial is currently underway although given the three year follow up period required prior to publication results are not anticipated imminently.

Subsequent management and prognosis

Changing concepts in management of the spina bifida patient, advances in neonatal, neurosurgical, urological and orthopaedic care have impacted on not only survival but on the quality and functional abilities of long term survivors. Any study of functional outcome in adult life clearly reflects the standard of early care two decades or more previously; however, by examining the literature pertaining to the various disciplines that impact upon the child with myelomeningocele some indication of contemporary prognosis becomes possible.

Survival

In the absence of additional serious congenital anomaly, children born with myelomeningocele are now likely to survive. In Lorber's original series 75 of 200 (37.5%) died in the first year of life (Lorber, 1972). In a somewhat later, unselected British cohort (Hunt, 1990) the rate of mortality at the first year was 25 of 117 (21%). Of 101 children born with myelomeningocele and treated at Great Ormond Street from 1997, there has been one death in the first year of life. A mean survival of 30 years has been estimated for patients with myelomeningocele (Davis *et al.*, 2005; Hunt, 1997). Ventriculitis and shunt related complications have previously been the prime causes of death during infancy; however, it is now brainstem dysfunction (due to the Chiari II malformation) leading to respiratory impairment and swallowing dysfunction that constitutes the majority of early deaths (Bowman *et al.*, 2001; Stevenson, 2004). Through childhood, adolescence and into adulthood mortality remains significant—25% overall mortality at 25 years in a large proactive myelomeningocele programme (Bowman *et al.*, 2001). This study corroborates the message from previous studies that shunt malfunction, often unrecognized remains a common, potentially avoidable, cause of death in older patients (Davis *et al.*, 2005; Hunt, 1990). In the majority of long term follow up studies, it is the renal complications that have been the commonest cause

of death for patients who survived into adulthood (Singhal and Mathew, 1999; Woodhouse, 2008).

Hydrocephalus

Hydrocephalus has often been considered an almost inevitable sequel of myelomeningocele and shunt placement rates in the order of 80–90% are commonly quoted in the neurosurgical literature (Bowman *et al.*, 2001; Rintoul *et al.*, 2002; Steinbok *et al.*, 1992). Where there is overt clinical and radiological evidence of hydrocephalus the decision to treat is straightforward. For the 15% of infants with clear evidence of hydrocephalus at birth, placement of a ventriculoperitoneal shunt can be performed simultaneously with the myelomeningocele repair. There does not appear to be any significantly increased risk of shunt infection when the shunt is placed at the time of myelomeningocele repair when compared with delayed shunt placement (Chaddock and Reding, 1988; Parent and McMillan, 1995). Where there is only moderate ventricular enlargement the decision to shunt should be deferred.

Placement of a shunt imposes a significant burden for the child in the future. Shunt dependent hydrocephalus and shunt related complications are not only detrimental to cognitive outcome (Barf *et al.*, 2003) but are strongly related to long term survival (Davis *et al.*, 2005; Hunt *et al.*, 1999; Oakeshott and Hunt, 2003; Tuli *et al.*, 2003; Tuli *et al.*, 2004). Shunt revision rates for this population are high (Bowman *et al.*, 2001; Steinbok *et al.*, 1992). In a study by Calderelli, 46% of shunted myelomeningocele patients required shunt revision in the first post operative year, approximately three quarters of these being due to mechanical failure (Calderelli *et al.*, 1996). Furthermore shunt infection rates are reportedly higher for myelomeningocele patients than for other hydrocephalus groups (Tuli *et al.*, 2003). There is thus good reason to avoid shunt placement where possible and in recent years it has been our policy to have a more circumspect approach with respect to shunt placement, accepting moderate ventriculomegaly and even some post operative increase in ventricular size which will frequently stabilize without intervention. Adopting such criteria, shunt placement rates have been reduced to 52% (Chakraborty *et al.*, 2008). It is clearly imperative that these children be followed closely to ensure that there is no cognitive cost of this policy.

Chiari II malformation

The neuroanatomical consequences of myelomeningocele extend well beyond the local spinal cord dysplasia. The majority of cases have the constellation of abnormalities in the brain that constitute the Chiari II malformation. These are most evident in the hindbrain where there is caudal displacement of the posterior fossa contents into the upper cervical canal, the fourth ventricle is small and the tectum is 'beaked' (Figure 1), however, forebrain anomalies such as interdigitation of the cerebral sulci and enlargement of the massa intermedia of

the thalamus are also commonly found. At a histological level the brainstem nuclei have been shown to be disordered, (Gilbert *et al.*, 1986) further supporting the concept that this is a true 'malformation' of the central nervous system (CNS) in sharp contrast to the unrelated Chiari I 'malformation' which is more a herniation or deformation of the normal cerebellum through the foramen magnum in response to local forces.

The Chiari II malformation is present in almost all myelomeningocele patients and is responsible for symptoms in between one fourth and one third. McLone has stated that it is the Chiari II malformation and its effects that determine the quality of life for the child with myelomeningocele (McLone and Dias, 2003). In the infant, central apnoea and lower cranial nerve dysfunction are common manifestations whilst in the older child and young adult symptoms of foramen magnum impaction such as neck pain, headache and sensory disturbance in the limbs are more common. Symptoms of apnoea, stridor (indicative of vocal cord paresis) and swallowing difficulties in infancy are associated with high mortality rates, up to 15% of symptomatic cases dying by the third year (Stevenson, 2004). Untreated or inadequately treated hydrocephalus may aggravate symptoms and simply correcting this can resolve symptoms in the majority of patients (Charney *et al.*, 1987; La Marca *et al.*, 1997). Whether or not early hindbrain decompression significantly improves on the natural history of this condition remains controversial as treatment related morbidity and mortality are high with mortality of 15–20% even in experienced centers (Pollack *et al.*, 1992; Vandertop *et al.*, 1992). Surgical mortality rates are considerably lower in older children and adolescents and thus for the symptomatic older child, hindbrain decompression is a treatment option but only once adequate shunt function has been confirmed.

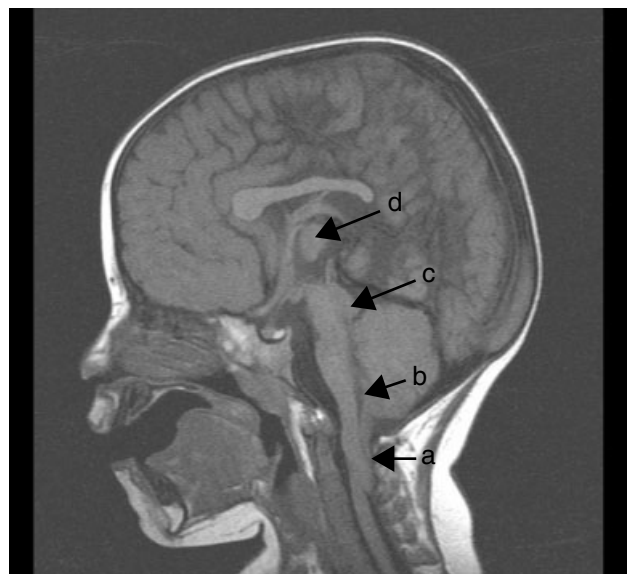


Figure 1—Chiari II malformation. The features include (a) elongated brainstem that extends into the cervical spinal canal; (b) small fourth ventricle; (c) tectal beaking; (d) large massa intermedia

Ambulation

In the absence of severe developmental delay (approximately 13%) the prospects for independent mobility are strongly related to the neurological level of the lesion. For low lumbar and sacral lesions, independent mobility is to be anticipated for almost all cases. For lesions above L2, loss of quadriceps and iliopsoas muscle function means that independent mobility is unlikely and parents should anticipate a wheelchair existence for such children (McDonald *et al.*, 1991; Seitzberg *et al.*, 2008). Whether, in addition to spinal level, the presence or absence of a myelomeningocele sac demonstrated prenatally has any prognostic significance has been suggested though not proven (Wilson *et al.*, 2007).

Early input from physiotherapy and orthopaedics is essential if optimal motor outcome is to be achieved (Swank and Dias, 1992). Through adolescence and into adulthood the proportion of ambulant patients decreases. This is commonly attributed to factors such as increasing weight, spinal and foot deformity, respiratory compromise each of which increase the physical effort of walking making use of a wheelchair a more efficient option (Bruinings *et al.*, 2007). In the long term outcome study of Oakeshott and Hunt only 30% of a cohort of 117 were ambulant at 30 years follow up, 88% of these had an initial level at L5 or below (Oakeshott and Hunt, 2003). In a more recent, albeit smaller series Seitzberg *et al.* (2008) reported that 52% of 52 myelomeningocele patients surviving to adulthood were ambulant in the community without walking aids, a further 21% were ambulant with aids. All patients with sacral level myelomeningocele remained ambulant.

Urological outcome

Urinary incontinence with its associated social stigma and damage to the upper urinary tract (due to reflux nephropathy and recurrent urinary tract infections) was previously a common feature of this condition. Indeed death due to renal failure was a major source of mortality in earlier series (Eckstein *et al.*, 1967). Whilst treatment of the underlying neural dysplasia responsible for the neurogenic bladder remains elusive, advances in urological management have led to significant clinical benefit (Figure 2). During infancy the principle aims of urological management are protection of the upper urinary tracts and control of urinary tract infection. In a recent retrospective audit from our own series early identification of the high risk child (history of urinary infection, small trabeculated bladder, ureteric/pelvic dilatation) followed by close clinical/radiological surveillance and early institution of catheterization dramatically reduced the incidence of new renal scarring and need for urgent surgical intervention (Desai unpublished data). Achieving continence is a later goal. The introduction of clean intermittent catheterization, the use of anticholinergic drugs to improve bladder capacity and aggressive management of constipation have significantly improved the urological prognosis both in terms of reducing the risk

of renal damage (Dik *et al.*, 2006) and achieving continence. Social continence (freedom from incontinence in social situations with or without clean intermittent catheterization) can now be achieved in as many as 80% of children (Bowman *et al.*, 2001; Kessler *et al.*, 2006; Steinbok *et al.*, 1992). What of future developments? Surgical procedures to increase bladder capacity are now commonly used in this population, however the usual technique of augmenting the bladder with a segment of intestine is associated with a number of short and long term complications. Recent publications have shown the possibility of using tissue culture techniques to create an autologous engineered bladder construct (Atala *et al.*, 2006). A further exciting possibility is the restoration of some degree of urinary continence by using nerve grafting to reinnervate the lower urinary tract. Xaio and colleagues in both animal and human studies have taken a healthy motor lumbar nerve root and grafted this on to a more distal sacral root to reinnervate the bladder. After successful grafting cutaneous stimulation of relevant lumbar dermatome then produces contraction of the bladder and thus voiding (Xiao, 2006).

Sexual activity in myelomeningocele patients is reduced for both male and female patients (Cass *et al.*, 1986; Verhoef *et al.*, 2005). This is related not only to the impaired neurological innervation of the genitalia but also to the detrimental effects of factors such as negative self image and incontinence anxieties. Sexual sensation and ability to achieve orgasm is again related to neurological level. For levels below L2, sexual sensation is likely to be intact particularly in cases where urinary continence is maintained. Only 20% of cases with a level above L2 or those with urinary incontinence will have retained sexual function (Cass *et al.*, 1986).

The increased length and quality of survival of women with myelomeningocele has meant that some have gone on to conceive and carry pregnancies through to term. Abnormal pelvic capacity, urological complications and premature labor have been shown to impact significantly on obstetric and anesthetic care (Richmond *et al.*, 1987; Rietberg and Lindhout, 1993). In addition, there is the risk to the fetus of having a neural tube defect which is approximately 4%. This risk can be reduced

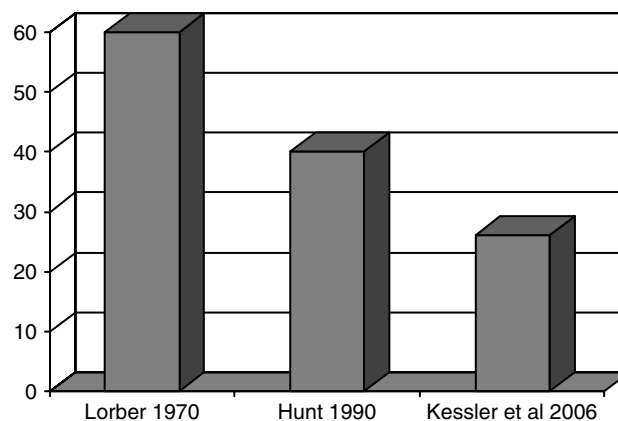


Figure 2—Percentage of myelomeningocele patients failing to achieve “social” continence.

with appropriate preconceptual folate supplementation. It is thus important that where possible appropriate counseling ought to be offered prior to conception.

Spinal deformity

Spinal deformity of some degree is present in approximately half of young adult spina bifida patients. The causes are multifactorial and include spinal bony anomaly, neuromuscular imbalance, spasticity together with pelvic and hip deformity (Dias, 2005). Severity of scoliosis and thus the need for surgical intervention is related to neurological level. In the Chicago series 86% of patients who required spinal fusion had a thoracic lesion (Bowman *et al.*, 2001).

Tethered spinal cord

A frequently overlooked and potentially treatable cause of deterioration in myelomeningocele patients is spinal cord tethering. Following the initial surgical repair the terminal spinal cord remains low in the spinal canal, commonly imbedded in scar tissue. As spinal growth continues, traction is exerted on the spinal cord and nerve roots leading to ischaemic injury and secondary neurological deterioration (Yamada *et al.*, 2004). In fact not only motor but urological deterioration, pain and progressive foot and spinal deformity may also ensue—the so called ‘neuro-orthopaedic syndrome’. Early recognition of this process and timely surgical intervention to untether the spinal cord can lead to significant improvement (Hudgins and Gilreath, 2004).

Cognitive outcome

Overall approximately 70% of myelomeningocele patients will have an IQ of 80 or more (Oakshott and Hunt, 2003). As noted above hydrocephalus and shunt related complications (blockage and infection) impact negatively on the cognitive outcome of children with hydrocephalus. In a Dutch study of young adults undergoing a range of neuropsychological assessments approximately half of the myelomeningocele population with hydrocephalus exhibited some impairment in cognitive functioning. By contrast, for those without hydrocephalus results were not dissimilar to the general population (Barf *et al.*, 2003).

In a study by Hunt approximately half of the patients surviving to adulthood were living independently either with no adaptations or in suitably adapted accommodation. The remainder required supervision or were wholly dependent for daily care (Hunt, 1990).

Data regarding the prospects for gainful employment is limited. Hunt estimated the capability to work amongst 69 adults with myelomeningocele and concluded that with the appropriate employment opportunities, home support and transport facilities only 25% were capable of open employment. A more recent Swedish study showed that 38% of adult survivors were in active employment

compared with 47% for traumatic paraplegia (Valtonen *et al.*, 2006).

ENCEPHALOCELES

Cranial neural tube defects occur much less commonly than their spinal counterparts. The prevalence of encephalocele is considered to be between 1 in 2000 and 1 in 5000 live births (Gorlin *et al.*, 2001). However, there is significant geographic variation, the incidence being particularly high in Asia.

Encephaloceles are part of a spectrum of clinical entities thought to result from disordered closure of the anterior neural tube. Whether these conditions are a true failure of neural tube closure or whether they are a post neurulation defect, a reopening of an already closed neural tube, has been questioned. This spectrum of ‘cranial dysraphisms’ comprises, at one end cranial dermal sinuses (persistent ectodermal connections between the skin and the meninges) and true encephaloceles (cranial defects through which meninges and variable amounts of brain tissue herniated) at the other. Between these extremes are meningoceles (cranial defects associated with herniation of a meningeal sac containing CSF but no neural tissue) and atretic meningoceles (small, nodular, non cystic lesions, commonly at the vertex). For meningoceles, atretic meningoceles and cranial dermal sinuses the underlying brain is usually structurally normal, the prognosis for these lesions is extremely favorable and normal or near normal development can be anticipated.

Neural tube closure has traditionally been considered to begin in the cervical region and then proceed rostrally and caudally from this point. Contemporary opinion is that fusion of the edges of the folding neural tube in fact occurs at a number of points along the length of the neural tube—the multisite hypothesis (Van Allen, 1996). This would be in keeping with the relatively consistent sites of encephalocele occurrence.

Encephaloceles are classified according to their anatomical location; frontal, parietal and occipital (Figure 3). In the western world the occipital variety is most common, whilst in Asia the frontal location predominates. Whilst most commonly occurring in the midline temporal and parietal encephaloceles are well recognized however these are extremely rare.

The prognosis for encephaloceles is largely dictated by three variables: anatomical site, volume of neural contents and the presence of coexisting malformations (cerebral and extracerebral).

Site

The more rostral along the neuraxis cephalocele the better is the prognosis. In an outcome study of 44 cranial encephaloceles occipital location carried a worse prognosis. Hydrocephalus and seizure disorders were more common in this group, approximately half of this group being significantly disabled and unlikely to live independently (Bui *et al.*, 2007).

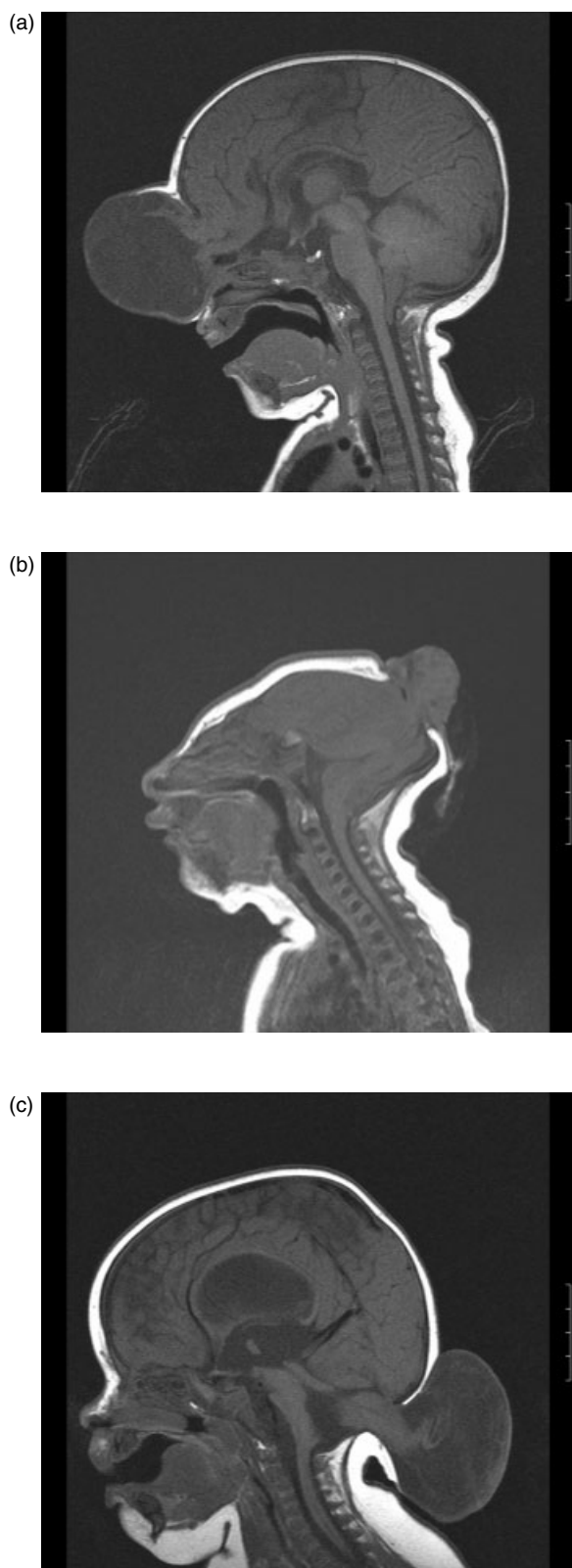


Figure 3—(a) Frontal encephalocele. There is frontal lobe within the sac, the rest of the brain is well preserved; (b) Parietal encephalocele. There is microcephaly and major brain malformation; (c) Occipital encephalocele. The brainstem is malformed and the dysplastic cerebellum extends into the sac of the encephalocele

Contents of sac

Large herniations of brain tissue into the cephalocele frequently with associated microcephaly generally portends a worse prognosis (Date *et al.*, 1993; Martinez-Lage *et al.*, 1996; Simpson *et al.*, 1984). Again this is in part related to site, as this reflects the eloquence of the brain tissue involved. Herniation of frontal cortex may be tolerated well whilst involvement of posterior fossa structures and brainstem is associated with increased morbidity and mortality.

Associated malformations

Coexisting intracranial anomalies are common in children with encephalocele of all types (Martinez-Lage *et al.*, 1996). These include parenchymal anomalies (e.g. neuronal migration disorders, intracranial cysts), ventricular anomalies (asymmetry, hydrocephalus) and vascular anomalies (falcine venous sinus, abnormal torcula). The presence of a severe intracranial anomaly worsens prognosis. In almost all studies the presence of hydrocephalus has been correlated with poor outcome (Bui *et al.*, 2007; Date *et al.*, 1993; Martinez-Lage *et al.*, 1996).

Whilst encephaloceles may occur in isolation they may also feature as part of a recognized syndrome of congenital malformation. These include chromosomal abnormalities (e.g. trisomy 18), single gene defects and teratogenic influences such as warfarin embryopathy. Well documented is Meckel syndrome, an autosomal recessive condition comprising polydactyly, polycystic kidney, holoprosencephaly, microphthalmia, retinal dysplasia and cardiac anomalies. Amniotic band syndrome is also associated with atypical forms of encephalocele where facial clefting and limb deformities may coexist. The presence of additional congenital abnormalities is associated with a poorer prognosis (Brown and Sheridan-Pereira, 1992).

Surgical treatment of parietal and occipital encephaloceles is usually straightforward with few complications. Frontal lesions may require more complex craniofacial techniques, however with appropriate treatment the majority of children born with encephalocele will survive and for those with frontal, small parietal or atretic encephaloceles, the prognosis is generally favorable. By contrast, occipital lesions particularly containing large amounts of cerebral tissue and where which are associated with microcephaly or hydrocephalus, are likely to have significant developmental delay.

CONCLUSIONS

Neither myelomeningocele nor encephalocele can be considered simple diagnostic labels. For each there is an extremely wide range of prognosis ranging from normality through to severe cognitive and physical disability. There has been a tendency for prenatal counseling to be unduly negative, failing to recognize the heterogeneity of these conditions and the impact of contemporary postnatal management. Prognosis is

largely dictated by anatomical site, extent of CNS tissue involved and the presence of coexisting conditions and so this underpins the importance of accurate prenatal diagnosis.

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