Multiple Neural Tube Defect: Encephalocele and Lumbosacral Myelomeningocele. Case report and literature review

Defeitos Múltiplos do Tubo Neural: Encefalocele e Mielomeningocele Lombossacra. Relato de caso e revisão da literatura

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ABSTRACT
Double neural tube defect is a rare congenital problem. We report a case and discuss about current theories of neural tube closure. A 39 weeks term baby with occipital encephalocele and lumbosacral myelomeningocele is reported and her management is described. A single-staged surgery was performed. The present case is the first described in South America and seems to support a multi-site closure theory.

Key words: Spinal dysraphism; Neurulation; Multi-site closure theory; Encephalocele; Myelomeningocele.

RESUMO
Defeito duplo do tubo neural é um problema congênito raro. As teorias disponíveis do fechamento dos tubos neurais são resumidas e comparadas com o caso descrito. O caso de um bebê a termo de 39 semanas com encefalocele occipital e mielomeningocele lombossacra é relatado juntamente com o seu manejo. Um procedimento cirúrgico foi realizado em tempo único. O presente caso, o primeiro descrito na América do Sul parece dar suporte à teoria de fechamento de múltiplos sítios.

Palavras-chave: Disrafismo espinhal; Neurulação; Teoria de fechamento de múltiplos sítios; Encefalocele; Mielomeningocele.

INTRODUCTION
Neural tube defects (NTD) are a great group of heterogeneous and complex congenital anomalies of Central Nervous System (CNS). In this group we found anencephaly, spina bifida and encephalocele. Several of neural and non-neural malformations are commonly associated with NTD1,10. The most frequent anomaly in open NTD are anencephaly and spinal dysraphism. Those malformations arise during neurulation. It occurs at 17th and 30th day after fertilization. NTD arising as a result of a primary failure of the neural tube closure are clinically apparent by being open, i.e. leaving tissue of the unclosed neural tube exposed, in contrast to postneurulation NTD, which are skin-covered4. Neurulation is the step in neural tube development where we see a thickening of the ectoderm from the level of the primitive node of Hensen caudally to prochordal plate rostrally at the beginning of the 3rd week of embryonic life. During the neural induction, in higher vertebrates, it is seen an inhibition of BMP-4 (Bone Morphogenetic Proteins) and involves an intricate interplay of FGF (Fibroblast Growth Factors), Noggin, Chordin, Wnt-3, Beta–catenin and possibly calcium transients12,15,29. Differential rates of cell proliferation, cell movement and changes in cell shape in the neural plate result in the formation of neural groove in the median plane and neural folds on the either side. By complex processes of cell-shaping, cell movement and cell adhesion, aided by the forces provided by the underlying mesenchyme and overlying surface ectoderm,
the neural folds elevate themselves, converge along the dorsal midline and fuse with each other to form the neural tube\textsuperscript{5,6}.

As in the case reported, occipital encephalocele comprises 70%-80% of all encephalocele cases\textsuperscript{3}. Besides the surgical treatment enhance substantially survival rate, individuals with lumbosacral myelomeningocele continue to experiment varying degrees of motor and sensory dysfunctions of the lower limbs and failure of anal and urethral sphincters. Essentially, all individuals with thoracic myelomeningocele and most of lumbosacral dysraphism are at increased risk for hydrocephalus and Chiari type II malformations\textsuperscript{23}.

**CASE REPORT**

Here we report a case of a female baby, born in Manicoré, State of Amazonas, a Brazilian Indian, with 39 weeks of pregnancy. Her mother did the prenatal exams and made only one Transvaginal Ultrasound exam in the first trimester. The child was delivered by vaginal natural birth. During the first medical evaluation it was identified a lumbosacral myelomeningocele associated to an occipital encephalocele. Then, she was sent to Manaus, the capital of the State for evaluation and surgery.

The child came into an ambulance breathing normally, moving the 4 limbs, but presented with paresis of the ankle, strength 2/5. A CT skull was performed and showed an Occipital Encephalocele 6.5 x 4.5 x 4.4 cm. myelomeningocele had 4.5 x 3.0 cm. The birth weight was 2,020 g at 1 day of life.

At the first day of life, the patient was taken to the operating room for immediate repair of both lesions, the myelomeningocele and encephalocele at one-staged surgery. The closure of the placodium and dural repair was performed. Then the cutaneous suture was done. After closing the lumbosacral myelomeningocele, the neurosurgery team performed the occipital encephalocele closure. The sac was opened and the resection of the herniated brain with primary duroplasty and skin repair was started.
After surgery, the patient remained hospitalized in the Pediatric Intensive Care Unit. She was extubated 2 days after surgery. The team was accompanying the cerebral perimeter for hydrocephalus that didn’t evolute. The neurological exam was the same before surgery. She was kept breathing with a Hood mask for three days more and started oral feeding in the 4th post-op day.

**DISCUSSION**

In the 2nd week after fertilization we have a rostro-caudal axis development. The primitive streak is formed after the epiblast cells migration to the midline. The primitive knot AKA Hensen’s node lies at the cranial end of the primitive streak. This elongates and encompasses the caudal end of the embryo. Then, gradually it regresses and the cells within Hensen’s node form the midline notochordal process. This has a central notochordal canal and then intercalates with the endoderm to form the notochordal plate, thus causing the amniotic cavity and the yolk sac to communicate through the primitive neurenteric canal. The ectoderm has two distinct forms: the centrally located neuroectoderm surrounding Hensen’s node and the rostral half of the primitive streak and the peripherally located cutaneous ectoderm. The centrally located neuroectoderm forms the nervous system.
Between the days 16 and 26, the neuroectoderm undergoes several changes to form the neural tube. These changes are called “Neurulation” and divided as primary and secondary. During the primary neurulation (days 18-26) a midline neural groove appears. The adjacent neural folds elevates dorsal and medially converging to form the neural tube. Once these folds fuse, the neural tube separates from the cutaneous ectoderm thus completing the process.

Here there have been 2 theories of neural tube closure. The conventional theory on the ethiogenesis of MMC is that it results from defective closure of the caudal neural tube between 26 and 28 days of pregnancy. The “single site closure theory” postulates that closure starts like a zipper from a single site, and moves bidirectionally, cranial and caudally. According to this theory, however, there would be only two sites of the anterior and posterior neuropores. However, this does not explain the full range of anomalies seen in humans.

Multiple sites of initiation of neural folds fusion was reported in the mouse by Sakai (1989) and later by others authors. In 1993, Van Allen et al. proposed the “Multisite Closure” of the neural tube theory. Their theory was based on the observation on therapeutic abortuses and still born fetuses who had fusion defects at different sites along the neural axis. In this theory it is postulated that there are 5 sites of closure (sites 1-5) and the defects of the neural tube could result from any problem at any of these sites.

The closure follows an order previously defined. Initially it begins at site 4 followed by sites 2 and 3, then sites 1 and 5. It is believed that the majority of neural tube defects could be explained by failure of fusion of one of these sites.

The pathologies according to complete failure of closure (based on multi-site closure theory) are shown in Table 1.

<table>
<thead>
<tr>
<th>Site</th>
<th>Clinical Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Closure 4</td>
<td>Occipital Encephalocele</td>
</tr>
<tr>
<td>Closure 4 and 2</td>
<td>Parieto-occipital Encephalocele</td>
</tr>
<tr>
<td>Closure 3 or 3 and 2</td>
<td>Frontal Encephalocele</td>
</tr>
<tr>
<td>Closure of 4 and 1 or rostral 1</td>
<td>Cervical Myelomeningocele</td>
</tr>
<tr>
<td>Caudal closure 1</td>
<td>Thoracolumbar Myelomeningocele</td>
</tr>
<tr>
<td>Closure 5 and 1</td>
<td>Lumbar Myelomeningocele</td>
</tr>
<tr>
<td>Closure 5</td>
<td>Lumbosacral Myelomeningocele/Lipoma</td>
</tr>
</tbody>
</table>

Though it has been postulated that anencephaly and spina bifida are primary closure defects and encephalocele are post-closure defects. A primary closure defect results in a midline encephalocele. So, this theory explains better the Multi Neural Tube Defects when compared to the conventional theory, the “Zipper-Theory”. There are other investigators like Nakatsu et al. (2000) and Martinez-Frias, in 1996, who also supported the Multi-Site Theory. Nakatsu et al. supported this theory after studying human embryos. It is believed that the type of neural tube defect affects the intrauterine survival of abnormal embryos. Almost all the embryos at 5 weeks which had total dysraphism died, just like those with opening lesion at rhombencephalon at 6.5 weeks. At 7 weeks, only those embryos who had defects in frontal and/or parietal regions survived.

Analyzing the literature, less than 1% of the Neural Tube Malformations were multiple. Only 9 cases of double neural tube defect and a single case of triple neural tube defect have been described in the world literature. Encephalocele was present in 4 cases; this is an extremely rare defect, probably because they die before birth. The authors believe that large encephalocele might have been aborted. Mealey et al. reported that only 4 patients had both encephalocele and myelomeningocele in a series of 623 patients analysed. It is also know that VATER syndrome and Knobloch syndrome are associated with occipital encephalocele and myelomeningocele.
CONCLUSION

We have described a very interesting and rare case. It takes part of a very uncommon neural tube defect. The embryogenesis of neural tube defects remains a matter of debate. The multi-site theory, though having a few drawbacks, explains much better the embryogenesis of the neural tube defects.

REFERENCES

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Não há conflito de interesses