Fetal repair of myelomeningocele in human fetuses. Experience related with 33 cases

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Abstract
Authors report the experience with fetal surgery due to meningomyelocele. Between 2005 and 2010 39 fetal surgeries were performed. Analysis was conducted on the basis of 33 children. From among 33 operated fetuses we have reported 6 deaths. Majority of children were born prematurely. Respiratory disorders were observed in 22 neonates, 16 newborns required mechanical ventilation, and 6 needed CPAP respiratory support. 26 from among operated children revealed spontaneous movements within lower limbs, to a various extent. 7 neonates between 30 and 172 day of life required implantation of valve system due to increasing hydrocephaly. Prenatal surgery for myelomeningocele reduced the need for shunting and improves motor outcomes but was associated with maternal and fetal risks.

Key words: meningomyelocele, fetal surgery, hydrocephalus

Possibility to observe fetal development on the ultrasound image resulted in extensive development within the new medical branch, namely fetal diagnostics and therapy. Due to prenatal diagnostics we can plan the proper date and manner of delivery, conduct the labor in a chosen center, which is best for the neonate, and agree with parents on the optimal manner of proceedings after birth. In certain, selected cases fetal therapy may be undertaken. Fetal interventions were begin to be conducted in situations, when diagnosed defect lead equivocally to fetal death. Such surgeries were preceded with a series of experimental researches performed on animals. These studies were performed mainly in the United States, and Michael Harisson, MD, specializing in pediatric surgery was a pioneer in these surgeries. He was the one to perform the first operation on an open uterus in 1982. This surgery was related with creating a cystostomy in fetus with posterior urethral valve in 1982 [12, 13, 15, 19].

Development in fetal therapy, and most of all the safety of the mother resulted in the fact that physicians began to consider interventions in fetuses, which did not have any lethal defects, but their therapy after birth did not prevent fixed disability [3,16].

Myelomeningocele is an example of such defect. Currently binding theory concerning the origin of this defect assumes that it is created within two stages /two hit theory/. During the first stage, between 4th and 8th week of fetal development we can observe disorders within spinal cord rolling. The second stage leads to secondary damage of the uncovered spine resulting from disadvantageous activity of the amniotic fluid and mechanical injuries of the spinal cord caused by contact with wall of the uterus. Only the fetal operation could prevent the above. Studies confirmed benefits resulting from closure of myelomeningocele created experimentally in test animals. First surgeries of myelomeningocele in fetal humans were performed by Scott Adzick in Philadelphia [3, 21]. The most considerable series of operated fetuses was presented by Brunner from Nashville [5-7].

Basing on American scientific publications, as well as exchange of personal experiences with doctor Brunner, repair of myelomeningocele in human fetuses were initiated in 2005 in Gynecology and Obstetrics Department in Bytom in cooperation with a team of pediatric surgeons from Paediatric Surgery and Urology Department in Katowice, Upper Silesian Child’s Health Center in Katowice [18, 23].

The aim of the thesis was to present the course and results concerning intrauterine therapy of human fetuses with prenatal diagnosis of myelomeningocele.

Material and method
Between 2005 and 2010 39 fetal surgeries were performed. Analysis was conducted on the basis of 33 surgeries executed between 2005 and July 2010.
Surgeries were realized between the 22nd and 30th week of pregnancy. Table 1.

Table 1. Gestational age at the moment of operation

<table>
<thead>
<tr>
<th>Hbd</th>
<th>Number of fetuses</th>
</tr>
</thead>
<tbody>
<tr>
<td>22-24</td>
<td>8</td>
</tr>
<tr>
<td>24-27</td>
<td>21</td>
</tr>
<tr>
<td>28-30</td>
<td>4</td>
</tr>
</tbody>
</table>

Location of hernia: lumbar spine – 3, lumbosacral – 21, sacral – 9.

Ethical Committee of Medical University of Silesia in Katowice gave consent to conduct the operation. Description of the “gynecological” part, including methods of anesthesia and tocolysis extends the scope of this thesis. Fetal operation was performed by pediatric surgeon with 4 × enlarging magnifying glass. Myelomeningocele is exposed after opening the uterus within the 10 cm wound. Surgery is being conducted according to principles binding in case of these types of operations in newborns. In majority of cases, the patient stays in hospital after the surgical procedure until delivery. Indications for the surgery: myelomeningocele opened below L3, appropriate karyotype, Arnold-Chiari syndrome in MRI imaging, lack of additional defects, complete acceptance of the mother and her close relatives to undertake fetal therapy.

Results

From among 33 operated fetuses we have reported 6 deaths. In one case placental abruption was reported during the surgery. Other children died because of prematurity, infection or as a result of associating defects (tetralogy of Fallot). Majority of children were born prematurely. The age at the time of birth was stated in table 2.

Table 2. Age at the time of birth

<table>
<thead>
<tr>
<th>Hbd</th>
<th>Number of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>27-28</td>
<td>3</td>
</tr>
<tr>
<td>29-30</td>
<td>8</td>
</tr>
<tr>
<td>31-32</td>
<td>4</td>
</tr>
<tr>
<td>33-34</td>
<td>8</td>
</tr>
<tr>
<td>35-36</td>
<td>7</td>
</tr>
<tr>
<td>38</td>
<td>1</td>
</tr>
</tbody>
</table>

Condition of children after birth (Apgar scale) was stated in table 3. Body weight after birth was stated in table 4.

Respiratory disorders were observed in 22 neonates, 16 newborns required mechanical ventilation, and 6 needed CPAP respiratory support.

Table 3. Condition after children after birth (Apgar scale)

<table>
<thead>
<tr>
<th>Number of children</th>
<th>Number of points</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>8-10</td>
</tr>
<tr>
<td>12</td>
<td>4-7</td>
</tr>
<tr>
<td>10</td>
<td>0-3</td>
</tr>
</tbody>
</table>

Table 4. Body weight after birth

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Number of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1000</td>
<td>6</td>
</tr>
<tr>
<td>1001-1500</td>
<td>10</td>
</tr>
<tr>
<td>1501-2000</td>
<td>5</td>
</tr>
<tr>
<td>&gt; 2000</td>
<td>11</td>
</tr>
</tbody>
</table>

Because of incomplete healing of the surgical wound 5 children required repeated operation after birth. 26 from among operated children revealed spontaneous movements within lower limbs, to a various extent. 7 neonates between 30 and 172 day of life required implantation of valve system due to increasing hydrocephaly. In three newborns valve implementation was preceded with Rickham collector installation. One child had ventriculostomy performed on 256 day of life.

Discussion

Referral of pregnant woman to the clinic initiated a procedure of preparing the woman for possible fetal surgery. During the initial stage patients sometimes reported quite late, which resulted in prolonging the preparatory process, hence 4 operations were performed between the 28 and 30 Hbd pregnancy. The patient, quite often assisted by her family (husband, mother) was informed in detail about the proposed therapy, including presentation of possible advantages, risks and possible complications. The patient stated her decision on the following day, so that she could have time to think and discuss the matter [4, 10].

The uterus was opened by a team of gynecologists, whilst the surgery on the fetus was performed by a team of pediatric surgeons. Fetal surgery required exposition of hernia within the lumen of open uterus within the segment of about 10 cm. There is no need to uncover the fetus from the uterus. When the placenta is located at the posterior wall it is possible to execute the surgery without emerging the uterus. Location of placenta on the anterior wall forced to take out the uterus and opening
Fetal repair of myelomeningocele in human fetuses. Experience related with 33 cases

It on the peak or the posterior wall. Location of the placenta and hernia is established by means of intraoperative ultrasound examination. It is extremely important to open the uterus as far as possible from the placenta. Manipulations close to placenta, touching it with hooks, etc. lead to the occurrence of hematoma or bleeding. In one case it lead to placental abruption and necessity to abort the operation. Quite often it turned out that opening of the uterus did not directly overlap the place where hernia was located and it was indispensable to turn the fetus. Since amniotic fluid flows after opening of the uterus, manipulations concerning the fetal position seem dangerous. Turning was performed with a finger of the operator and/or gauze pad on the tool (gauze tupfer). No fetal injury was reported. Nonetheless, this maneuver was extremely stressful. Fetal monitoring was performed by means of frequent placing the head of ultrasound device and evaluation of cardiac action, as the operators did not have at their disposal devices used in USA for constant supervision. No additional fetal anesthesia was used, according to an assumption that the anesthesia obtained by the mother will also act on the fetus. The fetus did not reveal any reaction in form of muscle contraction or changes within cardiac rhythm at the moment of initiating the procedure, or when performing the surgery. Some believe that it is essential to independently anesthetize the fetus [20].

Fetal surgery must be performed quite quickly. At the same time, exposure of operated part of the fetus is not always beneficial. That is why surgery cannot be performed in such an extensive manner, as it would be the case in neonates, especially in technically difficult forms. For example the occurrence of shifted skin-muscle-fascial lobe, which we often perform in neonates, seems impossible to be carried out in fetuses. Nevertheless, this hindrance is compensated by a greater tissue susceptibility to stretching than in neonates. Direct closure of hernia proved to be impossible only in two cases. In one case the operators used a patch from mother’s abdominal fascia, and in the second one – a Gore-tex patch. After the birth of these newborns the above-mentioned “transplants” were fully healed and there was no need to perform repeated surgery. In 6 cases the wound after fetal surgery was not tight and it was necessary to operate the baby after the birth. Records made by the operator do not allow to conclude a notion why the healing of a wound was worse. Quite often, when the reports stated that the operation was technically difficult, the wound was perfectly healed and the other way round. Premature labor constituted the most significant problem after fetal operation, which was also observed by other authors. [11]. The reason of the above is most probably related with premature flow of amniotic fluid. This was observed in 13 patients. The children were usually born before the 36th week of pregnancy. Neurological condition of children after fetal surgeries is under constant observations. However, it is not possible to equivocally state that this condition is better than after operating a newborn. What is worth mentioning, is the fact that occurrence of hydrocephaly decreased significantly. As far as the analyzed material is concerned, hydrocephaly requiring valve placement was observed only in 30% of children. This is inevitably the greatest benefit related with fetal surgery [1, 9]. Arguments in favor and against the fetal surgery of myelomeningocele are being constantly taken into consideration [8, 14, 17, 21, 22].

Arguments against include:

1) Lack of spectacular improvement concerning long-term results in comparison with operation performed immediately after birth.
2) Exposure of the mother to surgery, which would not improve her health.
3) This labor and all following ones need to be delivered by means of cesarean section.

Arguments in favor include:

1) Significant increase in frequency of hydrocephaly in children operated during fetal life.
2) It has not yet been unequivocally proved, but majority of children operated during fetal life reveal a better neurological condition.
3) Development related with new branch of medicine: fetal defects diagnostics and therapy.

Recently MOMS report has been presented in the Internet. Within its conclusion the authors state the following: Prenatal surgery for myelomeningocele reduced the need for shunting and improves motor outcomes at 30 month but was associated with maternal and fetal risks [2].

References


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