Congenital diaphragmatic hernia in dizygotic twins

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ABSTRACT

Congenital diaphragmatic hernia (CDH) is sometimes seen in siblings but is rarely seen in twins, and five survived cases of CDH in monozygotic or dizygotic twins have been reported in the English literature. Here we report a sixth survived case of CDH in dizygotic twins which was prenatally diagnosed as a very severe type and was successfully treated by our intensive care team composed of obstetricians, neonatologists, surgeons and anesthesiologists.

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The birth prevalence of congenital diaphragmatic hernia (CDH) is reported to be 3.3 per 10,000 births [1]. Among them, CDH cases occurring in both members of twins are extremely rare and only five pairs have been reported previously [2–6].

The etiology of CDH has usually been considered to be a sporadic event of development in most cases, but the involvement of genetic factors in its etiology cannot be completely excluded because there are some cases of CDH seen in relatives (mainly seen in siblings) [4,7,8]. In this context, CDH seen in twins is quite interesting and important, although rare.

We describe a sixth case of CDH seen in both members of twins. They were diagnosed prenatally as having a severe type and were treated successfully after birth.

1. Case report

A 38-year-old gravida 2 woman delivered a male and a female of dizygotic twins at 36 weeks' gestation by Cesarean section. Both twins had been diagnosed prenatally as having CDH at 29 weeks' gestation by the obstetricians in our hospital. Fetal ultrasound and MRI revealed the lesions as left-sided CDH with liver up and G3 (gastric position was mainly in the right thoracic space) [9] in both twins, indicating that they had the most severe type of CDH with pulmonary hypoplasia [9]. Aminocentesis was done and chromosomal anomalies were not detected in both fetus. There is no family history of diaphragmatic hernia and mother did not have any history to take some medications, smoking and alcohol intake during pregnancy. She also did not engage in any specific work to deal with some poisonous materials.

Twin A, a male patient, weighed 2188 g with Apgar scores of 3 e 4 and twin B, a female patient, weighed 2276 g with Apgar scores of 1 to 1 at birth. They had no deformity of extremities and no abnormal face, and were not detected any abnormality in central nervous system, kidney and heart, which indicated that the patients did not suffer from some syndromic disease. They were intubated immediately after birth and received intensive care with high-frequency oscillatory ventilation to obtain stabilization of respiro-circulatory systems. Their chest roentgenograms are shown in Fig. 1a and b. The mediastinum was shifted to the right side in both patients. After attaining stabilization of respiro-circulatory systems, twin A underwent curative surgery at 2 days of age. Twin B underwent...
curative surgery at 3 days of age although she had been stabilized the day before, so that the intensive care could be concentrated on each patient postoperatively. In operative findings of both patients, posterolateral hernia (Bochdalek hernia) was detected and their diaphragmatic defect involved about 75% of the left whole diaphragmatic area (defect C according to the definition by the CDH Study Group [10]) (Fig. 2a and b). In twin A the defect of the diaphragm was repaired with a Gore-tex patch, and in twin B the medial side of the defect of the diaphragm was partially closed by direct suture and the posterolateral defect was repaired with a...
Gore-tex patch (Fig. 3a and b). The postoperative recovery was uneventful. Both infants were discharged on the 107th day post-operatively without oxygen supplementation.

2. Discussion

To our knowledge, five survived cases of twins with Bochdalek hernia have been reported in the English literature [2–6] and our twins are the sixth. The characteristics of the six cases including ours are summarized in Table 1. Prenatal diagnosis was obtained in two cases, e.g., case 4 and ours. Four cases were monozygotic twins and two were dizygotic. All cases were affected by left-side diaphragm. In our twins, CDH was evaluated prenatally by ultrasonography and MRI, which revealed liver up (left lobe of the liver herniated into the thoracic space) [9] and L/T (lung to thorax) ratio < 0.08, which suggested that the cases were the most severe type, and the mortality rate at 90 days after birth in this entity was less than 50.0% [11]. After birth, two teams of intensivists cared for each patient respectively, whose pulmonary hypertension was very severe. We decided to perform surgical repair of the diaphragm in twin A first and on the next day twin B was operated, in order to provide full attention to the postoperative care for each patient. These considerations are needed in the care of CDH in twins.

The cause of CDH is generally thought to be a developmental occurrence rather than a genetic factor. However, a considerable number of familial CDH cases have been reported, although the true incidence of familial CDH cases is difficult to determine. A report of 143 sporadic cases and 58 familial cases of CDH revealed that males were more frequent than females in familial cases [3]. Hitch et al. [4] studied 141 siblings among 40 families in the literature and concluded that the inheritance mode must be autosomal recessive, but other authors have concluded that the inheritance mode for siblings with CDH is multifactorial [8]. Chromosomal analysis for the familial cases was reported in one paper and the results were negative for chromosomal abnormality [4]. The most recent review [12] documented the details of chromosomal abnormalities and gene abnormalities seen in CDH and most of them are associated with congenital anomalies including facial abnormalities, internal organ anomalies, deformities of extremities etc. These cases are called non-isolated CDH. In our case the patients had no such systemic anomalies and were considered as isolated CDH. Even now in most cases of non-syndromic CDH, the exact etiology is unclear and a new perspective to investigate it is needed. We now plan to perform the whole exome sequencing analysis to detect any mutations of the gene in our case and if any, it may make the etiology of the disease clear in the future.

In conclusion, CDH in both twin pairs has a very low incidence and the pathogenesis of this situation is still unclear. When the severe type of CDH is diagnosed prenatally in twins, we must prepare for the perinatal care in advance and also consider the proper timing of curative surgery in both patients for getting a satisfactory result.

Table 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Week</th>
<th>Weight (g)</th>
<th>Prenatal diagnosis</th>
<th>Zygote</th>
<th>Type of CDH</th>
<th>Stomach in thorax</th>
<th>Liver in thorax</th>
<th>Patch</th>
<th>Use of NO</th>
<th>Prognosis</th>
</tr>
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<tr>
<td>1</td>
<td>[4] Female</td>
<td>37</td>
<td>2170/2100</td>
<td>–</td>
<td>Monozygotic</td>
<td>Left/left</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Alive</td>
</tr>
<tr>
<td>2</td>
<td>[5] Male</td>
<td>34</td>
<td>2240/2100</td>
<td>–</td>
<td>Monozygotic</td>
<td>Left/left</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Alive</td>
</tr>
<tr>
<td>3</td>
<td>[6] Female/male</td>
<td>38</td>
<td>NA</td>
<td>–</td>
<td>Monozygotic</td>
<td>Left/left</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Alive</td>
</tr>
<tr>
<td>4</td>
<td>[7] Female</td>
<td>33</td>
<td>1587/1561</td>
<td>+</td>
<td>Monozygotic</td>
<td>Left/left</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Alive</td>
</tr>
<tr>
<td>5</td>
<td>[8] Female</td>
<td>37</td>
<td>2850/2000</td>
<td>–</td>
<td>Dizygotic</td>
<td>Left/left</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Alive</td>
</tr>
<tr>
<td>Our case</td>
<td>Male/female</td>
<td>36</td>
<td>2188/2276</td>
<td>+</td>
<td>Dizygotic</td>
<td>Left/left</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Alive</td>
</tr>
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NA – not available.

References