Treatment of congenital cystic adenomatoid malformation—does resection in the early postnatal period increase surgical risk?∗

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Received 7 September 2004; received in revised form 6 January 2005; accepted 17 January 2005

Abstract

Objective: The recent development of fetal ultrasonography has allowed for an increasing number of prenatal diagnoses for congenital cystic adenomatoid malformation (CCAM). However, the appropriate surgical timing of these patients has not been studied as of yet. The aim of this study is to suggest a safe strategy for the treatment of CCAM by identifying the relationship between the timing of surgery and postoperative outcome.

Methods: Between 1987 and 2003, 40 patients (28 males, 12 females) underwent surgical resection for CCAM. The mean age was 38.6 ± 9.1 (2 days–13 years) months. CCAM was diagnosed by prenatal ultrasonography in eight patients. Early operations were performed in four out of the eight. Operation was deferred until 2–12 months of age for the remaining four patients.

Results: Type I CCAM was found in 20 patients, type II in 20 and no patient exhibited type III. Five patients had associated pectus excavatum anomaly. There were no cases of operative mortality. Seventeen minor postoperative complications developed in 16 patients (40.0%): prolonged chest tube drain in 10, wound infection in 4, and 1 case of pneumonia, empyema and pleural space, respectively. The average hospital stay was 11.8 (6–29) days. During the mean follow-up period of 67.5 months, one patient died of accidental aspiration 7 months after operation during the postoperative recovery course of Ravich operation for pectus excavatum. The remaining patients reported doing well with normal physical activity. All five patients who underwent surgery at the age of under 1 month did not exhibit increased postoperative morbidity.

Conclusions: We concluded that surgery for CCAM could be safely performed in all age groups with satisfactory long-term outcomes. It is suggested that early elective surgical correction can be recommended for a patient whose diagnosis was made in utero.

Keywords: Congenital cystic adenomatoid malformation; Surgery; Complication; Early postnatal period

1. Introduction

Congenital cystic lung disease in children is uncommon. It can occasionally lead to a potentially life-threatening condition. Pulmonary sequestration, congenital cystic adenomatoid malformation (CCAM), congenital lobar emphysema, and bronchogenic pulmonary cysts are four major congenital cystic lesions in the lung and they share similar embryologic and clinical characteristics [1,2]. The incidence of CCAM has been reported in approximately 1 out of 25,000 pregnancies [3]. In some fetuses with this condition, nonimmune hydrops fetalis develops, resulting in fetal demise [4]. Others undergo spontaneous regression or resolution, with no evidence of the malformation at birth [5]. In contrast to the unknown postnatal course of CCAM, some research indicates that the prenatal clinical course of CCAM varies from the development of hydrops in as many as 40% of the cases to complete regression in 15% of the cases [6,7].

CCAM can be diagnosed prenatally by routine ultrasonography (USG). Although prenatal detection was made in limited early experiences, the recent advancement of fetal USG has allowed for an increased number of diagnoses of CCAM. However, in spite of recent developments of prenatal diagnosis of CCAM, the appropriate surgical timing for these patients has not yet been studied. Surgical resection is the standard management of symptomatic CCAM. However, the management of asymptomatic CCAM remains controversial [8–10]. The natural course of CCAM is not well known but a few complications, such as frequent infection, poor development of residual pulmonary function and possible malignancy, have been suggested. Therefore, many surgeons agree to resect the lesion in order to prevent those complications.

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The aim of this study is to suggest a safe strategy of early resection by identifying the relationship between the timing of surgery and postoperative results through a review of our surgical experiences of CCAM.

2. Material and methods

From November 1987 to June 2003, 40 patients (28 males and 12 females) underwent surgical resection for CCAM in our institute. The mean age at the time of operation was 38.6 months (2 days–13 years).

Eight patients were diagnosed prenatally by fetal USG and the remaining 32 were diagnosed postnataally. A chest CT exam was performed in each patient as a routine preoperative work-up and preoperative differential diagnosis was made according to the results of the chest CT exam. We did not perform a bronchoscopy as a routine preoperative test. None of the eight patients diagnosed by prenatal USG examination suffered from fetal distress and none required fetal intervention. Initial prenatal diagnoses made by fetal USG were CCAM in five patients, undefined mass in two, and congenital diaphragmatic hernia in one. Among them, four patients underwent early operation in the neonatal period, two as emergency-based and two as elective operations. Operation was deferred for the remaining four patients up to 2–12 months. Among the patient samples, five patients were operated on during the neonatal period and 35 patients underwent surgery at an older age.

Twenty-one patients (53%) showed no symptoms, 18 (45%) complained of frequent pneumonia or upper respiratory infection. Only one patient suffered from dyspnea.

Five patients had pectus excavatum and one had a bronchogenic cyst as an associated anomaly. The CCAM lesion was distributed evenly on both sides (right:left = 57.5%:42.5%, Fig. 1) and the lower lobes were more frequently involved (Fig. 1). Lobectomies were performed in 33 patients (82%) and segmentectomies were performed in 7 patients (18%). Lesions were classified according to the criteria proposed by Stocker: type I macrocystic, multiple large cysts; type II polymicrocystic, variable numbers of small cysts; type III homogeneous echogenic mass. Twenty patients had type I and 20 had type II. None of the patients were classified as type III. The medical records of the patients were reviewed retrospectively. The mean follow-up period was 67.5 months (1 month–16 years).

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Postoperative results were analyzed to identify the risk factors of poor outcome. Statistical analysis was done using Fisher’s exact test, Mann-Whitney test and logistic regression analysis with backward selection method. A P value of 0.05 or less was considered significant. The SPSS software, version 11.5 (SPSS Inc., Chicago, IL), was used for calculating statistics.

3. Results

Emergent or urgent operation was performed in five patients due to dyspnea or signs of increased cyst size with or without mediastinal shift. There were no cases of operative mortality. Among the five patients who had pectus excavatum, two received the Ravitch operation as a staged operation. One patient died at 7 months after lobectomy for CCAM; the death was caused by accidental aspiration that occurred during the postoperative recovery course of Ravich operation.

None of the patients experienced any major respiratory complications. Seventeen minor complications developed in 16 patients, which included 10 cases of prolonged chest tube drainage of air or fluids, 4 minor wound infections, and 1 case each of pneumonia, empyema, and pleural dead space. The duration of chest tube indwelling was 8.5 ± 5.9 (2–27) days. All of the wound infections were cured by conservative management. The patients who suffered from empyema and pneumonia recovered well with systemic antibiotics treatment and chest tube drainage. One patient who was dismissed with a small pleural dead space recovered well, and the space disappeared spontaneously on the chest PA film after a month.

To analyze risk factors for developing postoperative complications, we performed logistic regression analysis. Variables included gender, age, Stocker’s type of CCAM, presence of symptoms, presence of associated anomaly, emergent operation, and type of resection. Operations in older patients and emergency operations were significant risk factors for developing operative complications (Table 1). Table 2 compares the clinical characteristics of patients who were operated on at neonatal ages and those who were operated on at a later period. Patients who were diagnosed perinatally with USG and those who received emergency operations were more frequent in the early operation group. Other variables, such as type of CCAM, complication rates, duration of chest tube indwelling, and hospital stay, were not different between the two groups of patients. With the exception of the patient who died as

Table 1

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Odd ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Age (elderly, month)</td>
<td>1.025 (1.002-1.048)</td>
<td>0.030</td>
</tr>
<tr>
<td>CCAM type (type II)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Symptoms (present)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Associated anomaly</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Emergency operation</td>
<td>20.650 (1.650-258.458)</td>
<td>0.019</td>
</tr>
<tr>
<td>Procedure (lobectomy)</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Logistic regression, backward LR.

Fig. 1. Location of CCAM in 40 patients.
study developed complications when left untreated. They suggested that the non-operative approach might be a reasonable alternative for asymptomatic children with perinatally diagnosed CCAM because there was no increase in the postoperative complication rate even if surgery was delayed until the onset of symptoms [10]. We do not agree with their opinion. Their follow-up period was only 3 years and most of the patients were less than 5 years old when they analyzed the data. Another problem of conservative follow-up is the risk of malignancy in which true incidence is still unclear. A more practical problem is the method of follow-up. They recommended an annual follow-up of CT chest until adulthood. The patient may need frequent CT chest follow-ups due to the fear of developing either complications or unwilling malignancy even after childhood. It should be emphasized that surgical morbidity as well as mortality were low even in patients who were operated on relatively early during the postnatal period in their own study.

Our series demonstrated that every patient recovered fully from the operation with only minor complications; good long-term survival was achieved. From our experience, we can stress that all cases of asymptomatic CCAM can be removed with low operative morbidity. We operated on four patients during the neonatal period and had no cases of mortality. Although it may be too optimistic to conclude that all patients with CCAM can be operated safely during the neonatal period, as we experienced no major morbidity, we can say there appears to be no additional risk other than the risk operating in the neonatal period for patients with asymptomatic CCAM. In this context, we can conclude that surgery for asymptomatic CCAM may be safely performed in centers where neonatal surgery can be performed as routine procedure.

Focusing on the minor complications, operation at an older age and operation performed on an emergency basis resulted in an increased risk of complications. Emergency operations were performed when the patient showed signs of respiratory difficulty or when respiratory distress was expected during the follow-up studies. It is expected that those patients tend to have a more severe disease and thus will have poor outcomes. Although an emergency operation was a risk factor for developing complications, none of our emergency operation cases developed any significant respiratory complications. Two had minor wound infections, two had persistent chest tube drainage, and one experienced no complications. This satisfactory outcome seemed to be related with good patient selection. We decided to perform an operation if the patient showed any signs of respiratory distress or there was any evidence of the lesion progressing to develop symptoms. Among five emergency cases, only one patient suffered dyspnea and the remaining four were operated on an urgent basis as the lesion was too big or had increased in size, even though patients exhibited no symptoms.

An interesting finding is that complication rates increased with the patient’s age at the time of operation and the majority of complications were related to pleural space problems. The older patients were more likely to experience recurrent pneumonia and subsequent inflammatory sequelae on the pleural space may cause complications, especially related to the pleural space. However, as the odd ratio per month increase of age was only 1.024 (1.002-1.048),

### Table 2

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Early op (&lt;1 month)</th>
<th>Late op (&gt;1 month)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I/II</td>
<td>4/1</td>
<td>16/19</td>
<td>0.171</td>
</tr>
<tr>
<td>Associated anomaly</td>
<td>0 (0%)</td>
<td>6 (17%)</td>
<td>0.423</td>
</tr>
<tr>
<td>Fetal USG</td>
<td>4 (80%)</td>
<td>4 (11%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Emergency operation</td>
<td>4 (80%)</td>
<td>1 (3%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Complication</td>
<td>3 (60%)</td>
<td>13 (37%)</td>
<td>0.634</td>
</tr>
<tr>
<td>Chest tube indwelling (days)</td>
<td>8.4 ± 3.8</td>
<td>8.5 ± 6.1</td>
<td>0.712</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>12.6 ± 4.6</td>
<td>11.6 ± 5.8</td>
<td>0.435</td>
</tr>
</tbody>
</table>

* Fisher’s exact test, Mann-Whitney test.

previously described, all of the patients were doing well at the time of this study.

### 4. Comment

Recently, more and more developmental anomalies are being diagnosed prenatally by routine fetal USG. CCAM is one of the diseases frequently detected by fetal USG. Before the advent of prenatal ultrasound imaging, the diagnosis of CCAM had been made during the autopsy or an investigation of respiratory disease in childhood. When done by experienced obstetricians, CCAM can be accurately diagnosed and classified with exact Stocker’s type at 18–20 weeks of gestation. However, it is commonly reported to the thoracic surgeon as pulmonary cystic lesion or mass. In our study, only five out of eight cases were correctly reported as CCAM and we had to examine the patient with a chest CT scan after birth. There have been several reports about the intervention, such as percutaneous puncture or open surgery, during the fetal period. However, prenatal intervention is recommended only for fetuses that show the presence of hydrops because the risk of the procedure is high [7].

Davenport et al. [9] reported that antenatally diagnosed ‘cystic lung disease’ has an excellent prognosis in the absence of signs for severe fetal distress. They also stressed that the need for surgery should be determined by appropriate postnatal investigations and postnatal functional status, rather than by antenatal behavior itself. Traditionally, an emergency operation for CCAM is performed when the patient exhibits symptoms of respiratory distress in the neonatal period and subsequent diagnostic work-up reveals CCAM. In asymptomatic patients, the diagnosis of CCAM is not usually made until childhood or later, when symptoms of frequent pneumonia develop or an incidentally checked chest roentgenography reveals the lesion. In those patients, elective surgical resection is recommended at the time of diagnosis. There is, however, no clear indication for deciding the best timing for operation when the diagnosis is made in utero by fetal USG.

The development of neonatal care, thoracic surgical techniques, anesthesiology, nursing care, and postoperative management all enable safe surgery, even for a neonate. Therefore, many reports recommend early surgery for infants in all cases of CCAM [7]. However, Aziz et al. asserted that only 10% of asymptomatic CCAM lesions in their study developed complications when left untreated.
we suggest it would not cause a significant increase of risk even if the operation is delayed several months. However, waiting several years will result in substantial risk and such a long delay should be avoided.

Reported prenatal prognostic features for CCAM include the size and type of the mass, laterality, progression or regression of the mass, cardiac axis deviation, presentation with or development of hydrops, and the finding of other anomalies [11,12]. The development of fetal hydrops, as in most fetal disease states, is a poor prognostic factor. Fetal hydrops is thought to be the result of a mass effect caused by the volume of the CCAM. In our study, there were no cases of fetal hydrops. As for the size and type of the mass, Adzick et al. proposed a simpler classification of CCAM by fetal ultrasonographic findings. They divided the prenatally diagnosed CCAM into two groups (macrocystic and microcystic). Macrocystic lesions tend to be stable but can enlarge and most require postnatal surgical excision, whereas microcystic disease may diminish or resolve during pregnancy and, if so, can simply be followed up and investigated appropriately [13]. We were not able to classify the USG findings in such a manner as the USG had been performed in primary care hospitals, and we did not have such detailed data.

The extent of surgical resection is also controversial, but since most lesions are limited to the lobe, lobectomy is the mainstay surgical method. A more conservative policy of segmentectomy, when possible, seems to have been employed by some investigators [14,15]. However, this conservative surgery has several disadvantages, such as persistent air-leak or incomplete excision of the lesion. The type of resection, however, was not a risk factor in our study.

With regards to late complications, malignancies such as pulmonary rhabdomyosarcoma and bronchioloalveolar carcinoma have been reported, but this is currently unquantifiable [16-19]. In particular, rhabdomyosarcoma has been apparent during the childhood period and bronchioloalveolar carcinoma of CCAM in the fourth decade of life.

Based on this study, we have established a standard management strategy for prenatally diagnosed CCAM. After birth, the baby is transferred to the neonatal intensive care unit for careful monitoring. The next step is to obtain a chest CT scan. If the patient shows signs of respiratory distress, we recommend emergency operation. If the patient is asymptomatic and the chest CT reveals a large lesion with mediastinal shifting, we recommend urgent operation. If the baby is stable and the lesion is not large, we dismiss the patient with elective operation scheduled at 2-3 months of age.

5. Conclusion

Based on our experience, we concluded that surgery for CCAM could be safely performed in all age groups with satisfactory long-term outcomes. It is suggested that early elective surgical correction can be recommended for a patient whose diagnosis was made in utero.

References