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Laser therapy for type III fetal congenital cystic adenomatoid malformation

Laserová terapie pro vrozenou cystickou adenomatoidní malformaci plodu III. typu

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Summary: Congenital cystic adenomatoid malformation (CCAM) is a rare developmental anomaly of the fetal lung that can lead to severe respiratory distress in the neonatal period. Type III CCAM, characterized by solid, microcystic lesions, often poses diagnostic and therapeutic challenges, especially in progressive cases. We report a rare case of antenatal laser therapy used to treat a fetus diagnosed with type III CCAM. Despite two cycles of corticosteroid therapy, the lesion showed no significant regression, leading to the decision to perform ultrasound-guided intrauterine laser ablation. The procedure resulted in a reduction in lesion size, normalization of the fetal cardiac axis, and a favorable perinatal outcome, with the newborn discharged 5 days after birth in stable condition. This case highlights the potential role of fetal laser therapy as a less invasive and effective alternative to surgical excision for selected cases of progressive type III CCAM. Further studies are needed to validate the safety, efficacy, and long-term outcomes of this approach.

Key words: prenatal diagnosis – congenital cystic adenomatoid malformation – intrauterine therapy – ultrasound-guided laser ablation – perinatal outcomes

Souhrn: Vrozená cystická adenomatoidní malformace (CCAM – congenital cystic adenomatoid malformation) je vzácná vývojová anomálie plic plodu, která může vést k těžké respirační tísni v novorozeneckém období. CCAM III. typu charakterizovaná solidními, mikrocystickými lézemi často představuje diagnostické a terapeutické problémy, zejména v progresivních případech. Popisujeme vzácný případ prenatální laserové terapie použité k léčbě plodu s diagnózou CCAM III. typu. Navzdory dvěma cyklům nevykazovala kortikosteroidní terapie léze významnou regresi, což vedlo k rozhodnutí provést ultrazvukem naváděnou intrauterinní laserovou ablaci. Zákrok vedl ke zmenšení velikosti léze, normalizaci srdeční osy plodu a příznivému perinatálnímu výsledku, kdy byl novorozenec propuštěn 5 dní po narození ve stabilním stavu. Tento případ zdůrazňuje potenciální roli fetální laserové terapie jako méně invazivní a účinné alternativy k chirurgické excizi u vybraných případů progresivní CCAM III. typu. Pro ověření bezpečnosti, účinnosti a dlouhodobých výsledků tohoto přístupu jsou zapotřebí další studie.

Klíčová slova: prenatální diagnostika – vrozená cystická adenomatoidní malformace – intrauterinní terapie – ultrazvukem naváděná laserová ablace – perinatální výsledky

Introduction

Congenital cystic adenomatoid malformation (CCAM) is a type of congenital thoracic malformation that typically presents in infancy with respiratory distress caused by a space-occupying lesion that affects normal lung tissue. It was first mentioned briefly by Stoerk in 1897 and later detailed by Ch'in and Tang [1,2]. Early on, there was confusion about its relationship to other congenital lung cysts [3], such as bronchopulmonary sequestration, congenital lobar emphysema, bronchogenic cysts, and congenital bronchiectasis [4]. CCAM is characterized by cysts of various sizes lined by respiratory (bronchial-type) and cuboidal epithelium [5]. It constitutes 25% of all congenital lung anomalies and accounts for 95% of cases of congenital cystic lung disease. The incidence of prenatally diagnosed CCAM is estimated to be between 1 in 25,000 and 1 in 35,000 pregnancies [6]. In recent years CCAM was classified into five types by Stocker based on clinical and pathological features [7], the hypothesis being that these lesions range from type 0 being an essentially tracheobronchial defect to type 4 being an alveolar defect [8].

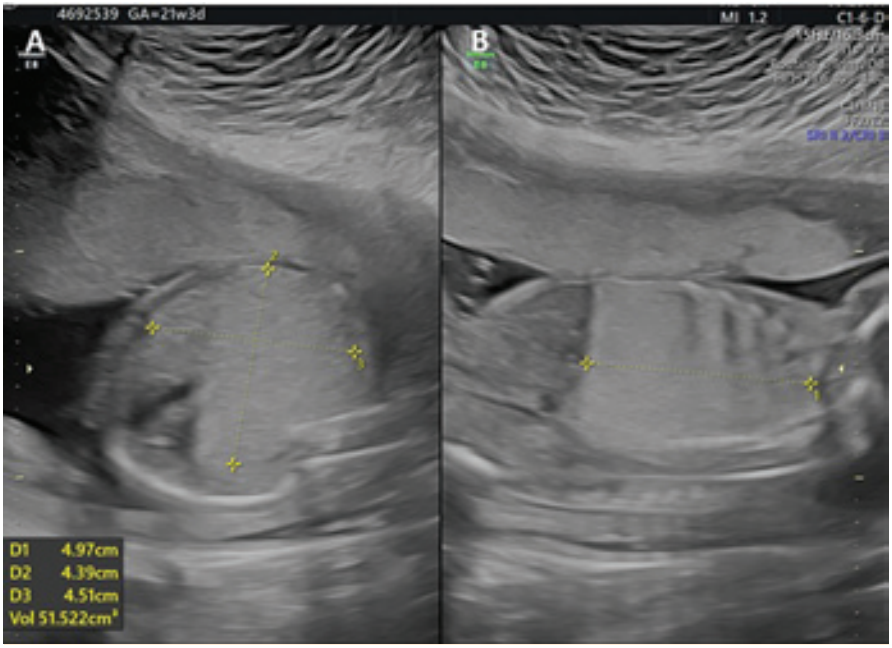

Fig. 1. Obstetrical ultrasound at thorax level in axial (A) and sagittal (B) views at 21 weeks of gestation showing the congenital cystic adenomatoid malformation volume calculation.
Obr. 1. Porodnický ultrazvuk na úrovni hrudníku v axiálním (A) a sagitálním (B) pohledu ve 21. týdnu těhotenství zobrazující výpočet objemu vrozené cystické adenomatoidní malformace.

CCAM is typically identified in the neonatal period or early childhood, with advances in diagnostics enabling prenatal management [7]. The standard treatment for CCAM is surgical excision, which helps prevent complications such as recurrent infections, pneumothorax, and malignancy. In this report, we present a case of type III CCAM treated antenatally with laser therapy targeting the lesion, rather than the conventional surgical excision. To our knowledge, there are very limited reports of this approach in the current literature.

Case report

A 35-year-old pregnant woman, of mixed ethnicity and married, with a history of two prior vaginal deliveries, underwent a routine obstetric ultrasound at 19 weeks and 2 days of gestation. The ultrasound examination, conducted at an external facility, revealed an echogenic mass occupying nearly the entire right hemithorax, measuring 28 × 25 × 24 mm (Fig. 1). The patient was referred to a fetal medicine referral center for further evaluation and management. Her 1st trimester scan had shown no abnormalities.

At the referral center, obstetrical ultrasound revealed a hyperechogenic mass occupying the entire right hemithorax, measuring 49 × 43 × 45 mm with a volume of 51.5 cm^3. No vascular connection between the aorta and the lung mass was identified. The heart axis was deviated to the left, and the leading diagnosis was type III CCAM. Differential diagnoses such as unilateral bronchial obstruction and pulmonary sequestration were initially considered but ruled out based on lesion characteristics.

The medical team administered two courses of betamethasone, three weeks

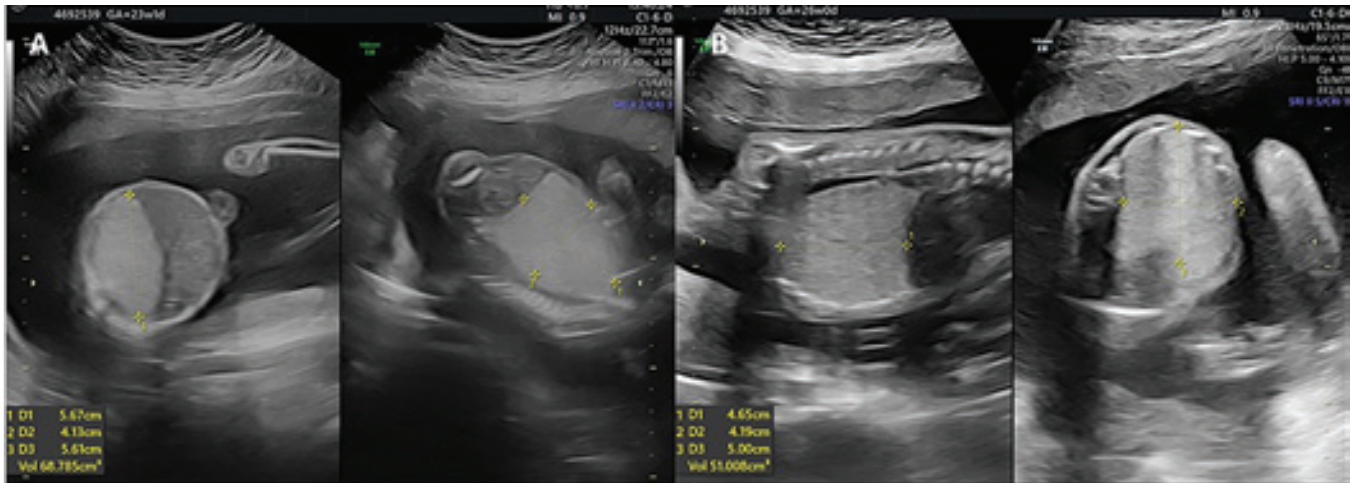

Fig. 2. Obstetrical ultrasounds at 23 weeks and 1 day (A) and 26 weeks (B), respectively, at thorax level in axial and sagittal views showing the congenital cystic adenomatoid malformation volume calculation after corticosteroid therapy.
Obr. 2. Porodnický ultrazvuk ve 23. týdnu a 1. dni (A) a 26. týdnu (B) na úrovni hrudníku v axiálním a sagitálním pohledu zobrazující výpočet objemu vrozené cystické adenomatoidní malformace po léčbě kortikosteroidy.

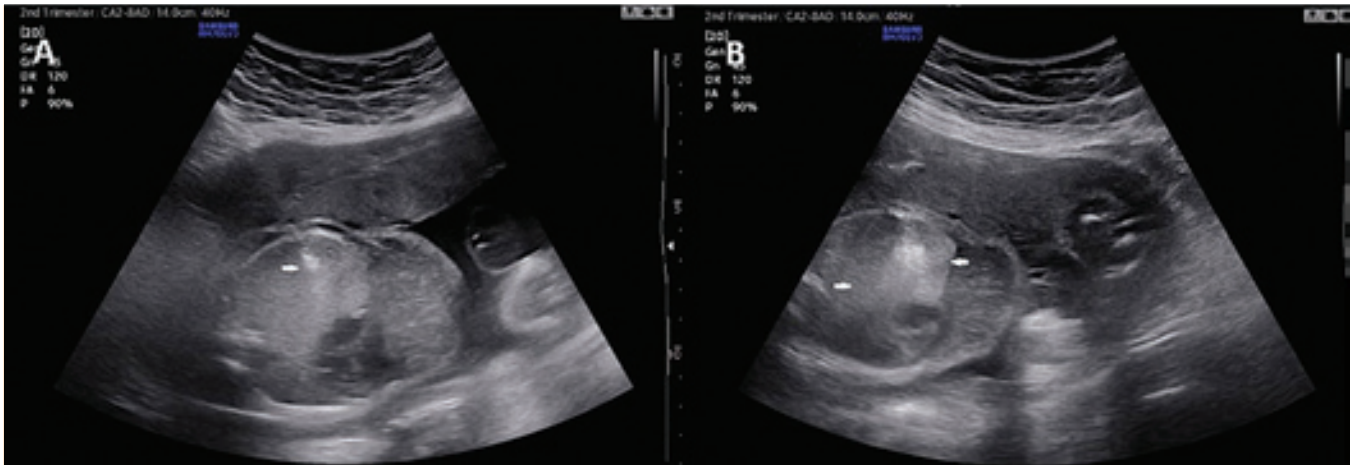

Fig. 3A) Ultrasound-guided laser ablation of congenital cystic adenomatoid malformation (arrow). 3B) Congenital cystic adenomatoid malformation image during the intrauterine therapy (arrows).
Obr. 3A) Ultrazvukem naváděná laserová ablace vrozené cystické adenomatoidní malformace (šipka). 3B) Snímek vrozené cystické adenomatoidní malformace během intrauterinní terapie (šipky).

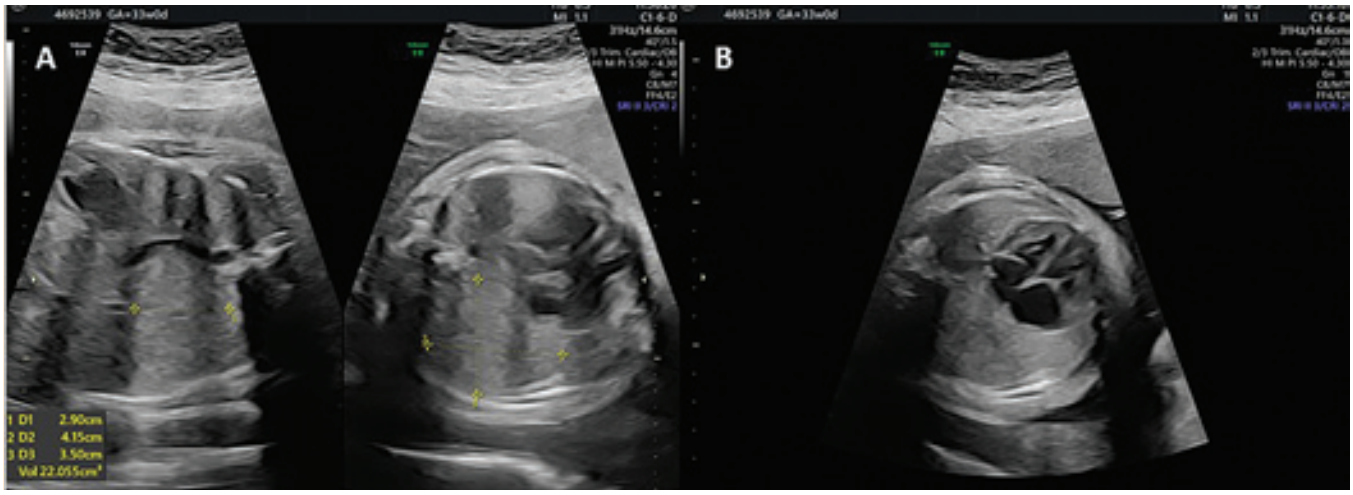

Fig. 4. Obstetrical ultrasound at thorax level in axial and sagittal views at 33 weeks of gestation showing the congenital cystic adenomatoid malformation volume calculation (A) and heart and lungs at the four-chamber view (B).
Obr. 4. Porodnický ultrazvuk na úrovni hrudníku v axiálním a sagitálním pohledu ve 33. týdnu těhotenství zobrazující výpočet objemu vrozené cystické adenomatoidní malformace (A) a srdce a plíce ve čtyřkomorovém pohledu (B).

apart. Follow-up obstetrical ultrasounds after steroid therapy showed lesion measurements of 56 × 41 × 56 mm (volume: 68.7 cm^3; CVR – congenital cystic adenomatoid malformation volume ratio: 1.99 without signs of edema or hydrops) and 46 × 41 × 50 mm (volume: 51.0 cm^3; CVR: 1.99) (Fig. 2). Due to the absence of a significant reduction in volume or CVR, fetal laser ablation guided by ultrasound was indicated 3 weeks after the second steroid course.

Under spinal anesthesia and sedation, the procedure began with antiseptic preparation and sterile draping. Fetal positioning was assessed by ultrasound for optimal lesion access. Uterine puncture was performed using an 18G needle, which advanced through the amniotic cavity to the thoracic region of the lesion. The needle stylet was removed and a laser fiber was inserted. Laser ablation was conducted at 5–10 Watts over 120 pulses, cauterizing the lesion's entire extent. The procedure was completed without complications (Fig. 3). Postoperatively, the patient remained hospitalized for observation for at least 24 hours and received symptomatic medication as needed. She subsequently attended weekly prenatal visits and obstetrical ultrasound assessments.

Postoperative evaluation revealed normalization of the cardiac axis, previously deviated to the left. The pulmonary mass, consistent with type III CCAM or unilateral bronchial obstruction, now measured 29 × 45 × 35 mm (volume: 22 cm^3) with a CVR of 0.73 cm^2 (Fig. 4). There were no signs of fetal edema or hydrops.

Spontaneous vaginal delivery occurred at 38 weeks of gestation at a hospital

with a specialized neonatal team present. The male newborn had an Apgar score of 9 and 10 at the 1st and 5th min, resp., and weighed 3,040 g, with an umbilical cord pH of 7.3. At 14 min of life, newborn presented with respiratory distress and was placed on continuous positive airway pressure (CPAP). Echocardiography revealed an atrial septal defect (foramen ovale type) measuring 7 mm. Chest computed tomography with contrast confirmed the diagnosis of CCAM in the right hemithorax, characterized by a radiolucent, multicystic lesion throughout the right lower lobe, with the largest cyst measuring 0.6 cm. The newborn was discharged five days postpartum with follow-up care scheduled with pediatric pulmonology, pediatric surgery, ophthalmology, and genetics teams. At this time, at one year of age, the infant remains asymptomatic.

Discussion

CCAM are cystic or sac-like lesions resulting from congenital abnormalities in the fetal lung that lead to dilations of the airways. Their incidence is estimated at approximately 1 in every 35,000 pregnancies. These anomalies involve changes in the respiratory epithelium and musculoelastic connective tissue, leading to abnormal development and, consequently, the formation of cystic areas. While some cysts are lined by bronchial-type epithelium, they lack all the typical elements of the bronchial wall, such as cartilage and mucoserous glands. These cysts also contain higher levels of elastic tissue compared to normal lung tissue. The coexistence of cystic lesions with adjacent normal alveolar structures suggests a developmental defect in lung regions that would typically give rise to terminal and respiratory bronchioles and alveolar ducts [5].

According to a 2017 literature review, there are four types of CCAM, initially classified by Stocker. Type I lesions are composed of large cysts – up to 10 cm – lined with pseudostratified epithelium, often localized to a single lobe. This type has a favorable prognosis and accounts for approximately 25% of cases, though it is the most symptomatic in the postnatal period. Type II lesions also account for about 25% of cases and consist of multiple smaller cysts (less than 5 mm) interspersed with areas of increased echogenicity on ultrasound. These are the most frequently associated with other congenital anomalies, particularly genitourinary and cardiac malformations. Type III lesions, representing approximately 50% of cases, appear solid macroscopically and non-cystic, but show microscopic microcysts smaller than 0.5 cm. These are generally asymptomatic [9,10].

In most cases, CCAM remain asymptomatic and stable throughout the fetal period. However, certain lesions can grow rapidly, peaking around 28 weeks of gestation. As they enlarge, they may compress the remaining pulmonary parenchyma, reducing lung expansion capacity and leading to respiratory distress. Additional complications include mediastinal shift and compression, polyhydramnios, postnatal pulmonary infections, and in severe cases, hydrops fetalis or anasarca. These conditions are associated with increased fetal mortality in the absence of therapeutic intervention [11,12].

The most common anomalies associated with CCAM are urogenital and cardiac malformations. Other associated abnormalities include tracheoesophageal fistula, cleft lip and palate, diaphragmatic defects, central nervous system anomalies, skeletal abnormalities, and other pulmonary malformations. When CCAM are found as isolated anomalies, genetic testing such as karyotyping is generally not indicated. After delivery, over half of the cases remain asymptomatic, although some newborns may experience respiratory distress [13,14]. A 2013 study reported that up to 41% of CCAM cases resolved spontaneously in utero by the third trimester, especially when the lesions were cystic or mixed. However, postnatal imaging with computed tomography still revealed residual lesions in nearly all newborns [12].

Fetal diagnosis is typically made through obstetrical ultrasound during the 2nd trimester, often supplemented with Doppler studies. Magnetic resonance imaging (MRI) and CT can also be used. An important prognostic measure is CVR, which calculates the lesion's volume using a specific formula: the lesion's dimensions multiplied by a constant (0.52) and divided by the head circumference. A CVR > 1.6 indicates a higher risk of hydrops and warrants increased monitoring and potential intervention [13,14].

Most CCAM cases are managed conservatively with regular fetal monitoring and no need for fetal intervention. Pharmacological treatment consists of two cycles of betamethasone at the same dosage used in standard lung maturation protocols. The maternal-fetal side effects are minimal. The effect of betamethasone on CCAM growth is variable, but favorable responses have been observed in cases with hydrops. These effects are attributed to a reduction in lesion size and acceleration of cystic maturation, although randomized studies are still needed to fully assess its efficacy [15]. The second-line treatment involves invasive fetal therapy, indicated for fetuses under 32 weeks of gestation with hydrops or a CVR > 1.6 who do not respond to corticosteroids. For macrocystic CCAM, available options include cyst aspiration via needle, thoracocentesis, thoracoamniotic shunting, ethanol ablation, or surgical resection via thoracotomy [16–18].

In cases of microcystic CCAM, fetal lobectomy via thoracotomy may also be beneficial. However, less invasive therapies are usually preferred initially – particularly for type III lesions – such as antenatal corticosteroid administration, especially when there is a high risk of hydrops. A few cases have been treated using laser ablation in microcystic or solid CCAM, with hydrops resolution

in four out of seven cases, although only two neonates survived postnatally. The first such study was conducted by Fortunato et al. [17], who observed normalization of cardiac axis and pulmonary growth following the procedure. A 2012 literature review suggested that laser therapy may benefit hydropic fetuses in particular [16–18]. There remains a scarcity of publications on the use of laser therapy for type III CCAM, likely due to the rarity of the condition and the limited availability of fetal surgery centers with the necessary resources and expertise.

Conclusion

This case report highlights the innovative use of laser therapy as an intrauterine treatment for type III CCAM. The intervention led to a reduction in lesion volume, normalization of the cardiac axis, and a favorable perinatal outcome, suggesting that this approach may offer a less invasive alternative for selected cases. While most type III CCAM cases are managed expectantly without fetal intervention, laser therapy may hold promise for progressive lesions – potentially minimizing neonatal complications and reducing the need for postnatal surgery. Further studies are needed to assess its efficacy, safety, and long-term outcomes.

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