

Congenital Cystic Adenomatoid Malformation Diagnosed During Adolescence

Zeynep Civelek¹, Nazan Dalgic¹, Canan Tanik², Sukru Mehmet Erturk³, Melih Akin⁴, Ihsan Kafadar¹

ABSTRACT:

Congenital cystic adenomatoid malformation diagnosed during adolescence
Congenital cystic adenomatoid malformation (CCAM) of lungs is a rare congenital lesion that is associated with abnormal proliferation of terminal bronchi and has an incidence of 1/4000 to 1/35000. Most of the cases (90%) are seen in the first two years of life and it is rarely seen in adolescents and the older age groups. Respiratory distress related to pulmonary compression and lung hypoplasia occur during the neonatal period, whereas recurrent and persistent pneumonia may occur at the older ages. The lesion is classified into five types by Stocker et al. Herein, we present a fourteen-year-old case who had no symptoms previously and diagnosed as type 2 cystic adenomatoid malformation with video-assisted thoracic surgery (VATS) due to persistent and treatment-resistant pneumonia.

Keywords: Adolescence, congenital cystic adenomatoid malformation, pneumonia

ÖZET:

Adolesan yaşta tanı alan konjenital kistik adenomatoid malformasyon

Akciğerlerin konjenital kistik adenomatoid malformasyonu (KKAM) terminal bronşiolerin anormal proliferasyonu sonucu gelişen nadir bir gelişimsel anomali olup insidansı 1/4000 ila 1/35000'dir. Olguların büyük çoğunluğu (%90) hayatın ilk iki yılı içinde tespit edilmekte ve ileri yaşlarda, özellikle adolesanlarda çok nadir görülmektedir. Yenidoğan döneminde pulmoner kompresyon ve hipoplaziye bağlı solunum sıkıntısı gelişirken daha büyük yaştaki olgularda rekürren ve persistan pnömoniler görülebilir. Lezyon Stocker ve arkadaşları tarafından 5 tipe ayrılmıştır. Burada daha önce hiçbir yakıması olmayan, tedaviye yanıtız persistan pnömonisi nedeniyle video yardımlı torasik cerrahi (VATS) yapılarak tip II kistik adenomatoid malformasyon tanısı alan 14 yaşında bir olgu sunulmuştur.

Anahtar kelimeler: Adolesans, konjenital kistik adenomatoid malformasyon, pnömoni

Ş.E.E.A.H. Tıp Bülteni 2017;51(3):247-51



¹Sisli Hamidiye Etfal Training and Research Hospital, Department of Child Health and Diseases, Istanbul - Turkey

²Sisli Hamidiye Etfal Training and Research Hospital, Department of Medical Pathology, Istanbul - Turkey

³Sisli Hamidiye Etfal Training and Research Hospital, Department of Radyodiagnostik, Istanbul - Turkey

⁴Sisli Hamidiye Etfal Training and Research Hospital, Department of Pediatric Surgery, Istanbul - Turkey

Address reprint requests to / Yazışma Adresi: Zeynep Civelek, Sisli Hamidiye Etfal Training and Research Hospital, Department of Child Health and Diseases, Istanbul - Turkey

E-mail / E-posta: zeyno_kcicek@hotmail.com

Date of receipt / Geliş tarihi: January 27, 2016 / 27 Ocak 2016

Date of acceptance / Kabul tarihi: April 1, 2016 / 1 Nisan 2016

INTRODUCTION

Congenital cystic adenomatoid malformation (CCAM), a hamartomatous lesion of the lung, is a developmental anomaly characterized by interrelated proliferating terminal bronchioles, cystic and solid structures. The incidence is 1/4000 to 1/35000, which accounts for 25% of congenital lung malformations and 95% of congenital cystic lung malformations. It is more common in men (1-3).

The etiopathogenesis is not fully explained and there is a lack of maturation in the proximal airways at 4th-8th gestational weeks, with an embryological

developmental disorder that is characterized by enlargement in the distal alveolar tissue (4,5). In 1977, there were 3 types (6), while in 2002, the classification has been expanded into 5 types by Stocker et al. According to this new classification, CCAM involves all pulmonary lobes and is incompatible with life in Type 0. Cases with Type I lesion constitute 60-70% of cases with CCAM. The cyst is single or multiple, with a diameter 2 cm and larger, and it's the best group in terms of life expectancy. Type II lesion is seen with a rate of 15-20%. There may be one or more cysts, 60% of cases are accompanied by additional anomalies,

primarily by renal agenesis or dysgenesis, cardiac anomalies and intestinal atresia. The diameter of the cysts is less than 2 cm and the life expectancy is around 40%. Type III lesions are the least common type (5-10%) with a life expectancy of 50%, a cyst diameter of less than 0.5 cm, and they are usually a solid lesion. In Type IV CCAM, the cysts are large, peripheral and thin-walled. Their prevalence is less than 10% and they are usually asymptomatic and diagnosed when they are admitted with spontaneous pneumothorax (7).

Herein, we present a fourteen-year-old case who had no symptoms previously, pre-diagnosed as pneumonia and tuberculosis and therefore diagnosed as type II CCAM.

CASE

A 14-year-old Mongolian male patient with no prior history of illness and hospitalization was brought to our emergency pediatric clinic with complaints of cough, fever and chest pain lasting for the last three days. Patient was admitted to our Pediatric Infection Department with a pre-diagnosis of pneumonia. On physical examination, medical

state was good, height percentile was 75-90, weight was 90-97, fever: 37.8°C, heart rate: 84/min, respiratory rate:16/min, he had diminished breath sounds in middle and lower parts of the left lung and crepitant rales. Other system examinations were normal. The patient had left lung lower lobe pneumonia on chest x-ray (Figure-1), and in the blood tests, leukocyte was 11450/mm³, neutrophil: 8700/mm³, CRP:135 mg/L (N: 0-5 mg/L) and other blood parameters were within normal limits.

Intravenous (iv) ceftriaxone 80 mg/kg/day was initiated in two doses. At approximately 48 hours of hospitalization, the chest X-ray of the patient with respiratory distress and continuing fever was repeated; thorax ultrasonography (USG) was performed due to the presence of effusion in the left lung. The thorax USG showed an effusion of 5.5 cm in the same area. A chest tube was inserted to the patient and the laboratory examination of the drained liquid material showed glucose to be 84 mg/dL, LDH: 766 U/L, protein: 4202 mg/dL, density: 1010, leucocyte: 55/mm³, erythrocyte:1500/mm³ and ADA: 46.3 U/L (N: 5-30 U/L). Mycobacterial PCR result was negative. Pulmonary computed tomography (CT) was performed because the pleural effusion receded and



Figure-1: Infiltration and pleural effusion in the middle and lower lobe of the left lung

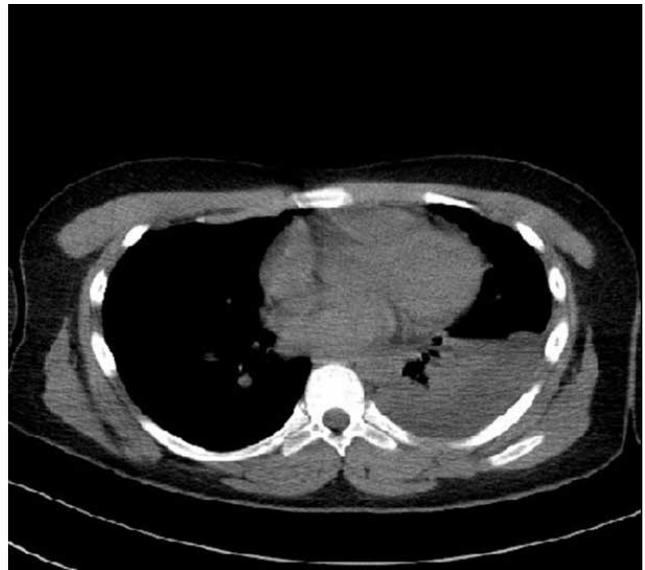


Figure-2: In mediastinal window section tomography of the lungs, pleural effusion in the basal segment of the left lung, and atelectasis in the adjacent lung parenchyma

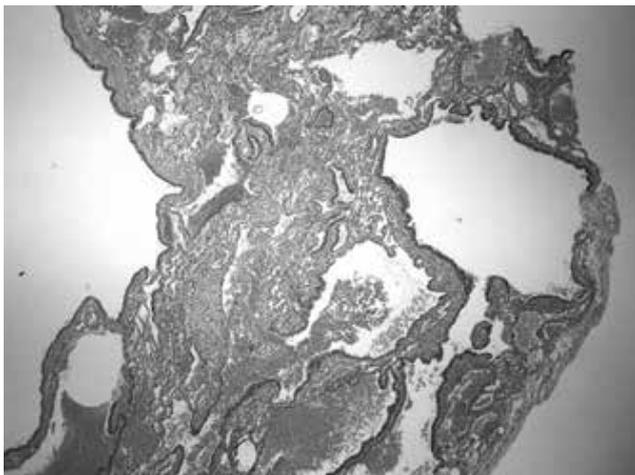


Figure-3: Small cystic structures in lung tissue with HEx100 magnification

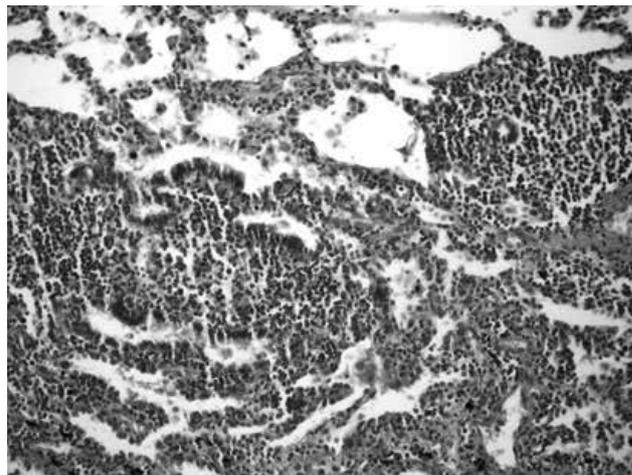


Figure-4: Small cystic structure in surrounding lung tissue and intense inflammation rich in lymphocytes with HEx200 magnification

the patient's fever still persisted on the third day of the thoracic tube removal. In CT; consolidation without air bronchogram in basal parts of the left lung, tree-in bud sign, atelectasis, and multiple localized calcifications in liver were detected (Figure-2). It was suggested to be compatible with tuberculosis (TB). Patients who were diagnosed as PPD negative and had no family history of TB were requested to have a family scan in terms of TB, but family members did not go to the tuberculosis dispensary for screening tests. The patient was tested for QuantiFERON-TB Gold; but the result was unclear. There was no growth in the results of the patient whose samples of gastric juice during starvation were tested on 3 consecutive days for the diagnosis of tuberculosis. He was consulted by the Department of Child Gastroenterology due to microcalcifications in the liver. It was stated that it might be tuberculosis, but due to the patient's ongoing fever, biopsy specimen couldn't be taken. Due to the ongoing high fever and pneumonia findings, the patient's current antibiotic treatment was stopped and piperacillin-tazobactam 4 gr/dose treatment was given iv in 4 doses. On the 14th day of intravenous antibiotic treatment, thorax tomography of the patient who had no fever was repeated; similar findings with the previous tomography were detected.

Video assisted thoracic surgery (VATS) and pleural and pulmonary samples were taken by Pediatric

Surgery for differential diagnosis from patients whose findings didn't improve and who had fever at least once a day. It was told by the Pediatric Surgery that there was intense abscess formation at the lesion site. The pathological examination was found to be consistent with congenital cystic adenomatoid malformation type II, and chronic nonspecific lymphocytic pneumonia and also mucinous goblet cells normally not seen in type II CCAM have been observed. Although pathologic examination was consistent with type II, the reason for the presence of mucinous goblet cells was thought to be normal bronchial and cartilage cells stuck in between (Figure-3,4).

The patient who was diagnosed as infected CCAM, treated with piperacillin-tazobactam for 3 weeks, and the fever going down, was admitted to the Pediatric Surgery Polyclinic to have the cystic lesion to be removed surgically in the lung under elective conditions. The patient was also taken under follow-up for the biopsy for microcalcifications shown in the liver. But since the patient did not have social security, he didn't show up for his follow-up visits.

DISCUSSION

Cystic disease of the lung was first reported by Bartholinus in 1687, and congenital cystic adenomatoid malformation of the lung was described

by Stoerk in 1897. Stoerk has reported his case as "cystic fetal bronchial adenoma" (8,9). The cases were compiled in 1949 by Chi and Tang, in 1964 by Belganger, la Fleche and Picard, and by Demster in 1969 (8). The great majority of cases (90%) are detected within the first two years of life and are very rare in older ages, especially in adolescents (2). Etiopathogenesis is not yet fully understood. There are no cartilages on the walls of cystic structures, and the internal surfaces are lined with cubic or columnar epithelium (10). Characteristically, they may be of varying shapes ranging from non-cartilaginous cystic formations to a solid mass. Elastic fiber organization around these cystic structures is frequently detected. Inflammation at the area with lesion is a rare finding in newborns, while frequently found in adults (1). CCAM is usually unilateral and limited to a single lobe. Our 14-year old case admitted to us with findings of pneumonia. Our patient had left lower lobe involvement.

There are five defined types of this disease of which the etiopathogenesis cannot be fully explained: Type 0: Acinar dysplasia, tracheobroncholar origin, Type I: Multiple large cystic type with bronchial/bronchiolar origin, Type II: Small cystic type with bronchiolar origin, Type III: Small cysts with bronchiolar/alveolar origin, Type IV: Peripheral cystic type with distal acinar origin. In 1977, Stocker (6) classified according to histological criteria and identified CCCAM as three types. In 2002, he renamed CCAM as 5 types by redefining Type 0 and Type 4 (7). In Type 0, the tracheobronchial tree and lungs contain solid and dense mesenchymal tissue and this type is incompatible with life, while Type 4 is the peripheral cysts originating from distal acinar. These may also interfere with bronchogenic cysts (6,7). CCCAM is usually unilateral and limited to a single lobe (11). According to Miller et al. (12), while the upper and lower lobes are involved equally, the involvement of the middle lobe occurs at a lower rate, and histopathologically, a large number of cystic structures stratified with a prismatic or cuboidal epithelium, showing anastomoses with each other and give terminal airways an adenomatoid appearance, are seen. There is another morphological finding which is remarkable, is the presence of elastic

fiber increase frequently around these cystic structures. Cartilage particles are not present in the cystic parenchymatous tissue other than the bronchiolum in the normal histological structure except for the diseased lung tissue. The inflamed area of the lesion is a frequent finding in adults and rarely seen in newborns, and normal parenchyma structure may exist between the cysts (6,7). This type is the most commonly seen and reported only in adults. Our case was also morphologically compatible with this form of Type 2.

In newborn cases, there is respiratory distress due to mass effect, pulmonary compression or hypoplasia. Symptoms are quite severe, especially when there is a lot of air trapping. However, in older cases, recurrences and persistent pneumonia can be seen. Half of the reported cases of adolescence and childhood admitted with fever and pneumonia symptoms. It is important that there is no radiological recovery after the treatment of pneumonia. Our patient also had a pneumonia that did not respond to antibiotic therapy, but after that, our patient was diagnosed with infected CCAM. The differential diagnosis of CCAM, which is very rare in adults, includes pneumatocele, cystic bronchiectasis, congenital lobar emphysema, intrapulmonary bronchogenic cysts. In pneumatocele, complex epithelial and stromal components are not present as in cystic adenomatoid malformation. There is no alveoli at the distance between the cysts in the lobar emphysema. Pulmonary sequestration may be excluded if there is no abnormal artery from the systemic circulation coming to the lobe that is involved, during the operation. Intrapulmonary bronchogenic cyst can be distinguished from the differential diagnosis by its placement in the hilar region, solitary formation, the presence of cartilage in the wall, and the absence of direct connection with the alveoli (1,13). In countries where tuberculosis such as our country is common, pulmonary tuberculosis should be considered in differential diagnosis. In our patient with persistent pneumonia, tuberculosis infection was suspected in the foreground, but we moved away from the preliminary diagnosis of tuberculosis by advanced examinations and biopsy.

The exact diagnosis of the disease is usually made after surgical resection and histopathological evaluation of the mass. CCAM can be detected at the intrauterine period by antenatal ultrasonography nowadays. Fetal hydrops, polyhydroamnios, pulmonary hypoplasia and mediastinal displacement are common secondary findings and poor prognostic factors. Lobectomy is preferred in the treatment. The prognosis is very good in young adults and children and in ones treated with pulmonary resection (2,14).

CONCLUSION

CCAM is a rare disease that causes pulmonary compression and hypoplasia leading to respiratory distress in the newborn. In young adults, recurrent or prolonged pulmonary infection is diagnosed with accompanying radiological findings. Therefore, in adolescents and adults with prolonged lung infection who are unresponsive to treatment, CCAM should be considered and histopathologic examination should be done for definite diagnosis.

REFERENCES

1. Avitabile AM, Greco MA, Hulnick DH, Feiner HD. Congenital cystic adenomatoid malformation of the lung in adults. *Am J Surg Pathol* 1984; 8: 193-202. [\[CrossRef\]](#)
2. Wilson RD, Hedrick HL, Liechty KW, Flake AW, Johnson MP, Bebbington M, et al. Cystic adenomatoid malformation of the lung: review of genetics, prenatal diagnosis, and in utero treatment. *Am J Med Genet A* 2006; 140: 151-5. [\[CrossRef\]](#)
3. Sahu S, Muthuvel S, Naware SS, Dhavala SS. Congenital cystic adenomatoid malformation of lung. *Medical Journal Armed Forces India* 2008; 64: 268-9. [\[CrossRef\]](#)
4. Gürsoy S, Yıldız S, Usluer O, Yazgan S, Başok O, Yücel N. Erişkin yaşa ulaşmış akciğerin konjenital kistik adenomatoid malformasyonu. *Türkiye Klinikleri Akciğer Arşivi* 2004; 5: 147-9
5. Lerullo AM, Ganapathy R, Crowley S, Craxford L, Bhide A, Thilaganathan B. Neonatal outcome of antenatally diagnosed congenital cystic adenomatoid malformations. *Ultrasound Obstet Gynecol* 2005; 26: 150-3. [\[CrossRef\]](#)
6. Stocker JT, Madewell JE, Drake RM. Congenital cystic adenomatoid malformation of the lung. Classification and morphologic spectrum. *Hum Pathol* 1977; 8: 155-71. [\[CrossRef\]](#)
7. Stocker JT. Congenital pulmonary airway malformation: a new name and an expanded classification of congenital cystic adenomatoid malformation of the lung. *Histopathology* 2002; 41(Suppl 2): 424-31.
8. Holder TM, Christy MG. Cystic adenomatoid malformation of the lung. *J Thorac Cardiovasc Surg* 1964; 47: 590-7.
9. Van Dijk C, Wagenvoort CA. The various types of congenital adenomatoid malformation of the lung. *J Pathol* 1973; 110: 131-4. [\[CrossRef\]](#)
10. Reynolds M. Congenital lesions of the lung. In : Shields TW (ed). *General Thoracic Surgery*. Philadelphia: Williams & Wilkins; 1994. p.870-4.
11. Aksoy F, Ramazanoğlu R, Şen C. Congenital cystic adenomatoid malformation type III associated with congenital anomalies. *Perinatoloji Dergisi* 2000; 8: 123-5.
12. Miller RK, Sieber WK, Yunis EJ. Congenital adenomatoid malformation of the lung A report of 17 cases and review of the literature. In: Sommers SC, Rosen PP (eds). *Pathology Annual (Part1)*. New York: Appleton Century Croft; 1980. p.387-407.
13. Bale PM. Congenital cystic malformation of the lung: A form of congenital bronchiolar ("adenomatoid") malformation. *Am J Clin Pathol* 1979; 71: 422-9. [\[CrossRef\]](#)
14. Cacciari A, Ceccarelli PL, Pilu GL, Bianchini MA, Mordenti M, Gabrielli S, et al. A series of 17 cases of congenital cystic adenomatoid malformation of the lung: management and outcome. *Eur J Pediatr Surg* 1997; 7: 84-9. [\[CrossRef\]](#)