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REVIEW / DERLEME

Congenital diaphragmatic hernia

Kongenital diyafragma hernileri

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ABSTRACT

Congenital diaphragmatic hernia (CDH) is a rare developmental defect of the diaphragm, characterized by the herniation of abdominal contents into the chest, resulting in varying degrees of pulmonary hypoplasia and pulmonary hypertension. Significant advances in the prenatal diagnosis and identification of prognostic factors have resulted in the continued refinement of the approach to fetal therapies for CDH. In the postnatal period, protocolized approaches to lung-protective ventilation, nutrition, prevention of infection, and early aggressive management of pulmonary hypertension have led to improved outcomes in infants with CDH. Surgical repair of CDH is not urgent in most circumstances and can be delayed until the pulmonary status of the patient has stabilized. This article provides a comprehensive review of CDH, focusing on the complex pathophysiology, advances in prenatal diagnosis, fetal interventions, and optimal postnatal management of CDH.

Keywords: Bochdalek hernia, diaphragm, Morgagni hernia, pediatric, surgery,

ÖZ

Konjenital diyafragma hernisi (KDH), çeşitli derecelerde pulmoner hipoplazi ve pulmoner hipertansiyon ile sonuçlanan, karın içi organların göğüs boşluğuna fıtıklaşması ile karakterize, diyaframın nadir görülen bir gelişimsel defektidir. Prenatal tanı ve prognostik faktörlerin tanımlanmasındaki önemli ilerlemeler, KDH'ye yönelik fetal tedavi yaklaşımının sürekli olarak iyileştirilmesine yol açmıştır. Postnatal dönemde akciğer koruyucu ventilasyon, beslenme, enfeksiyonun önlenmesi ve pulmoner hipertansiyonun erken agresif yönetimine yönelik protokollenmiş yaklaşımlar, KDH'li bebeklerde sonuçların iyileşmesine yol açmıştır. Konjenital diyafragma hernilerinin cerrahi onarımı çoğu durumda acil değildir ve hastanın akciğer durumu stabilize olana kadar ertelenebilir. Bu makale, karmaşık patofizyolojiye, prenatal tanıdaki gelişmelere, fetal müdahalelere ve postnatal yönetimine odaklanarak KDH'nin kapsamlı bir incelemesini sunmaktadır.

Anahtar sözcükler: Bochdalek hernisi, diyafragma, Morgagni hernisi, pediatrik, cerrahi.

Congenital diaphragmatic hernia (CDH) is a congenital anomaly of unknown etiology, characterized by the penetration of abdominal organs into the thorax cavity through an anatomical defect that occurs when there is a developmental defect in the muscle components of the diaphragm in the early fetal period.[1] It occurs approximately in every 3,000-5,000 live births and has high perinatal morbidity and mortality rates.[2] The most important causes of morbidity and mortality are association with other malformations, the degree of pulmonary hypoplasia, and the presence of secondary pulmonary hypertension.[2] According to their anatomical location, they are divided into three groups: posterolateral hernias (Bochdalek), retrosternal or parasternal hernias (Morgagni, Larrey), and central hernias that develop in the nonmuscular central tendinous part. Seventy to 75% of the cases are children with a left-sided Bochdalek hernia.[3] Some authors have reported that the incidence of CDH is slightly higher in male fetuses.[4] The majority of diaphragmatic hernias are diagnosed in the prenatal or neonatal period.[5]

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HISTORY

The first case of CDH was reported by Lazarus Riverius in 1679, following the autopsy of a 24-year-old male.[6] The first case of CDH in a child was reported by Holta in 1701. Cooper described the symptoms, pathology, and classification of CDH in 1827. Bowditch presented the first series of CDH patients at the Boston Society for Medical Observation meeting in 1847.[6] In 1848, Victor Alexander Bochdalek described the posterolateral hernia, which was later named after him.[7]

The first surgical treatment of CDH was made by Nauman in 1888, who performed laparotomy on a 19-year-old male patient with acute abdomen and acute respiratory distress.[6] This was followed by O'Dwyer's first surgical treatment of a child in 1889. The first successful surgical repair was performed in 1905. Heidenhain performed the reduction of the hernia of a nine-year-old child to the abdomen and closed the diaphragmatic defect with a midline laparotomy incision. Approximately 20 years later, Hedbolm reported a 58% mortality rate in patients undergoing surgery for CDH.[6] In 1940, Ladd and Gross made the diagnosis of CDH based on medical history information, physical examination findings, and the results of radiological examination of the lung with or without barium. They also recommended that surgery be performed within the first two days.[7] Gross also described the two-stage closure of the abdominal wall in difficult cases (skin and subcutaneous tissue in the first attempt, abdominal wall five to six days later). In 1950, Koop and Johnson proposed the transthoracic approach, which allowed repair under more direct vision.[8]

Areechon and Reid observed in the 1960s that the reason for the high mortality of CDH was related to the degree of pulmonary hypoplasia at birth. Extracorporeal membrane oxygenation (ECMO) was first successfully used in the treatment of persistent pulmonary hypertension in 1976. Later, ECMO also found a place in the treatment of CDH. In the last two decades, the importance of pulmonary hypertension and pulmonary hypoplasia in the pathophysiology of CDH has been demonstrated. Various recent studies have shown that cardiac developmental disorders complicate the pathophysiology of CDH.[8]

EMBRYOLOGY AND PATHOGENESIS

The diaphragm is derived from the septum transversum, the pleuroperitoneal folds, derivatives from the body wall, the dorsal mesentery, and a pair of premuscle masses lying opposite the fourth cervical segment of the 9-mm embryo. The septum transversum originates around day 22 at a cervical level but caudal to the developing heart. In normal conditions, the pleuroperitoneal folds fuse with the septum transversum, and the esophageal mesentery and the muscular ingrowth from the body wall invade the folds, forming the muscular part of the diaphragm. The complete development of the diaphragm should be completed by week nine, and the sealing of the left side occurs a week after the right. If a pleuroperitoneal defect persists at 10 weeks of pregnancy, the returning intestines may enter the thoracic cavity, usually on the left side, which is related to the earlier closure of the right pleuroperitoneal opening. Lung development normally occurs at 14 to 16 weeks of intrauterine life. Interference with normal lung development at this time results in decreased bronchiolar branching and pulmonary hypoplasia, as well as truncation and overmuscularization of the pulmonary arterial tree and pulmonary hypertension. Abnormal development of the lung also results in a dysfunction in the surfactant system late in gestation and after birth.[4]

The etiopathogenesis of CDH is unknown. In the beginning, it was believed that the defect was associated with failure of diaphragmatic closure. At present, it is postulated that a disruption occurs during lung development, as a first step towards the development of CDH, followed by the failure of diaphragmatic closure.[2]

ETIOLOGY

The etiology of CDH remains unknown in over 70% of individuals. In the vast majority of cases, CDH occurs sporadically without an identifiable familial link. However, in some cases, autosomal recessive, autosomal dominant, and X-linked inheritance patterns have been reported.[9] It was thought that some genetic and environmental factors may play a role in the emergence of the disease. There are some articles suggesting environmental triggers, such as vitamin A deficiency, as well as exposure to thalidomide or anticonvulsants, as possible causes.[10,11] Additionally, mycophenolate mofetil (immunosuppressive agent) and allopurinol have been associated with CDH due to impairment in purine biosynthesis.[12] They are also associated with some syndromes. Aneuploidies, such as trisomy 13, 18, and 21 and Turner syndrome, genetic syndromes, such as Fryns syndrome, and deletion, duplication, inversion, and chromosomal structural anomalies, such as translocation, are the genetic factors that are accused.[1] A brief summary of the etiological factors of CDH is given in Table 1.

DIAGNOSIS

A. Prenatal diagnosis: Prenatal diagnosis of CDH is based on prenatal ultrasonography (USG) screening. In the vast majority of cases, the abnormality is detected during routine anomaly screening, so the average gestational age at diagnosis is approximately 22-24 weeks.[14] Since the echogenicity of the fetal lung and liver are close to each other, in suspected cases, Doppler USG can be used to visualize the course of the ductus venosus and intrahepatic vessels.[15] Magnetic resonance imaging allows easy evaluation of liver herniation.[3] Polyhydramnios may occur in pregnancies with fetal CDH as a result of esophageal compression and fetal swallowing impairment. The risk of premature birth may develop due to polyhydramnios. In severe cases, hydrops fetalis may even occur as a result of mediastinal shift and compression of large vessels.[16]

B. Postnatal diagnosis: After birth, the baby's symptoms are determined by pulmonary hypoplasia and pulmonary hypertension. While in very severe cases, symptoms are observed immediately after birth, in most cases symptoms occur within the first 24 h. The most obvious symptoms are acute respiratory distress and cyanosis. On physical examination, there is a collapsed abdomen and an asymmetrical, fastigiate chest structure. Bowel sounds may be heard in the thoracic cavity. Mediastinal shift impairs venous return. As a result, hypotension and peripheral perfusion disorder develop. Observation of gas shadows belonging to the stomach and intestines in the thorax on direct radiograph is diagnostic. Additionally, seeing the nasogastric tube in the thorax cavity supports the diagnosis.[1]

Some patients have no symptoms, and a hernia may not be diagnosed for months to years. The presence of CDH is detected as a result of radiological examinations performed for another reason. Among the abdominal radiograph findings of children with late-diagnosed CDH, the gastric gas image, which is always observed in the left lower part of the diaphragm, is very useful. In CDHs affecting the left side, gastric gas is not visible in the abdomen. It may be found in an abnormal location in the abdomen or thorax.[8]

DIFFERENTIAL DIAGNOSIS

Congenital diaphragmatic hernia can most often be confused with congenital cystic adenomatoid malformations in the neonatal period.[1] Diaphragmatic agenesis is considered the most extreme form of CDH. Other thoracic lesions that should be considered in the differential diagnosis include bronchopulmonary sequestration, bronchopulmonary foregut malformation, bronchogenic cysts, bronchial atresia, enteric cysts, and teratomas.[17] At older ages, it may be confused with pathological conditions, such as diaphragm eventration, Morgagni hernia, hiatal hernia, congenital cystic diseases of the lung, pneumatoceles after empyema, and lung agenesis. Differential diagnosis can be made using direct radiographs and, if necessary, computed tomography (CT).[1] Table 2 shows the most common fetal lung lesions in differential diagnosis.

BOCHDALEK HERNIA

Definition and etiology

Bochdalek hernia is the most common type of diaphragmatic hernia and accounts for 95% of the cases.[18] It is encountered as a defect in the posterolateral side of the diaphragm due to the inability to close the pleuroperitoneal canal in 8-10 weeks of gestation. Varying degrees of pulmonary hypoplasia develop depending on the defect and the volume of the

Table 1. Etiological factors of CDH[4-13]

Type of factor	Example	Estimated frequency
Environmental	Vitamine A deficiency	Rare
Teratojenik drugs	Mycophenylate mofetil Allopurinol Lithium	Rare
Chromosome abnormalities	Trisomy 13 Trisomy 18 Trisomy 21	10-35%
Genetic syndrome	Fryns syndrome	<10%
Unknown	-	>70%

CDH: Congenital diaphragmatic hernia.

Table 2. The most common fetal lung lesions in differential diagnosis of CDH[4]

Type of lesion
Congenital cystic adenomatoid malformation (CCAM)
Bronchopulmonary sequestration
Diaphragmatic eventration
Teratoma
Bronchial atresia
Enteric cysts
Bronchopulmonary foregut malformation

CDH: Congenital diaphragmatic hernia.

herniated organs. The most important condition that determines the prognosis of patients is the degree of pulmonary hypoplasia. It occurs in every 2,000-5,000 live births. Although it is mostly observed on the left (80%), it can also be seen on the right or bilaterally. The size of the defect may be 1-2 cm, or the total absence of the diaphragm may be observed. According to different series, 15-50% of patients may have accompanying cardiovascular system, central nervous system, and chromosomal anomalies.[5]

Clinic

Severe respiratory distress occurs immediately after birth or becomes evident in the first days. Resuscitation in the delivery room may be required. Most babies are born at term. Congenital diaphragmatic hernia should be suspected in babies with a scaphoid abdomen and heart sounds heard on the right side immediately after birth. Tachycardia may be presented with dyspnea, tachypnea, and cyanosis. If the hernia is small, it may be asymptomatic and be diagnosed during other examinations and tests performed in childhood. Feeding difficulties and respiratory complications in children should be a warning. Rarely, it maybe silent until adulthood (Figure 1).[19] Silent hernias in adults are usually smaller than 4 cm and appear as retroperitoneal fatty tissue hernia. Again, the defects encountered in adults are mostly on the right side since the liver partially covers the defect, causing it to be asymptomatic and delaying diagnosis. These patients may also present with a chest wall mass, diarrhea, reflux, recurrent pneumonia, and recurrent effusion. In patients with known hernia, situations that create pressure changes, such as coughing fits or blunt trauma, may cause acute obstruction by allowing the stomach and intestines to pass into the thorax.[5]

Diagnosis

Hernia can be detected with prenatal USG. Seeing the liver inside the chest on prenatal USG indicates a poor prognosis. In the postnatal period, seeing bowel loops or a nasogastric tube placed for decompression in the thorax on a posteroanterior radiograph is a pathognomonic finding for diagnosis.

Treatment

The first successful prenatal surgical repair of a human fetus was reported in 1990. The repair was performed with a two-stage technique, including thoracotomy and subcostal incision to reduce the organs. Prenatal intervention is not recommended in cases of CDH that are not accompanied by liver herniation. Physiological intervention with fetal tracheal occlusion is a method that aims to control lung development by creating pulmonary hyperplasia and closing the trachea, ensuring that the lung fluid that triggers cell growth remains in the lung and increases vascularization.[8] On the other hand, it reduces the number of type 2 pneumocytes and surfactant expression. This is the reason for balloon removal at 33-34 weeks of gestation. Prenatal balloon removal is also associated with lower morbidity and better survival.[20] It is stated that severe isolated CDH cases (less than 25 weeks gestation) diagnosed prenatally will benefit from the fetal tracheal occlusion method if liver herniation is present.[8,21-23] Tracheal occlusion may also have some side effects for the fetus, and the most common is tracheomegaly, which has little or no clinical effect.[24]

If diagnosed in the neonatal period, the patient should be sent to a center with ECMO, similar to the one used in open heart surgery. Extracorporeal membrane oxygenation is used in neonatal respiratory failure, its success rate varies between 35-80%, and it provides oxygen and carbon dioxide exchange without affecting the lungs. Surgery should be performed after the need for ECMO is over. The baby should be stabilized for at least 72 h before surgery, and elective surgery should be planned. Preoperative surfactant treatment increases success. Surgical intervention is performed through a paramedian incision through the abdominal route. The herniated abdominal organs are pulled back into the abdomen, and the hernia sac is removed. If the remaining defect is small, it is closed primarily; if it is large, it is closed with a synthetic graft.[5] If the edges of the diaphragm are insufficient, the sutures are fixed to the rib cage or abdominal wall. When closing the abdomen, if it is thought that closing the

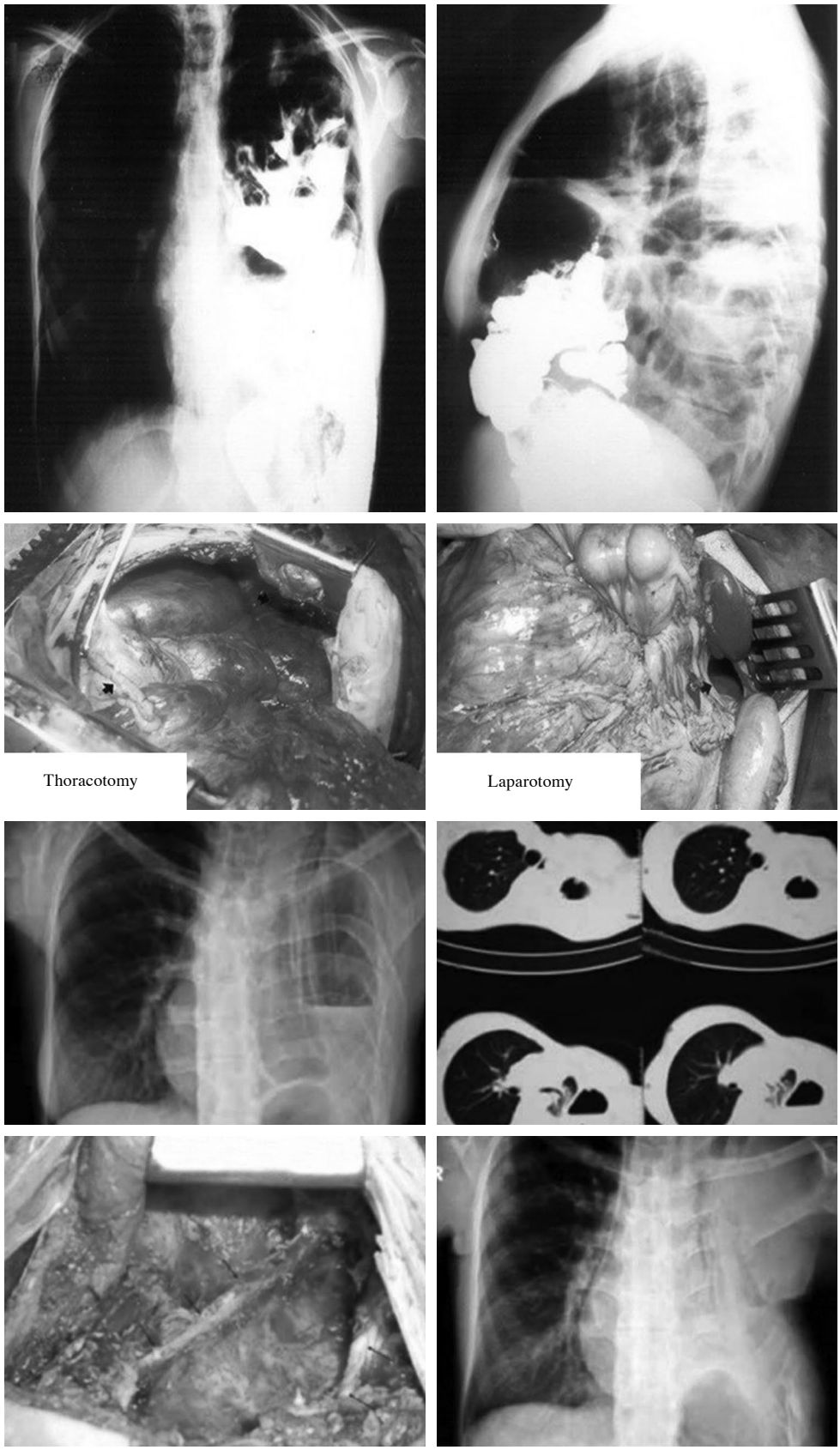

Figure 1. A case of Bochdalek hernia in adulthood.

fascia may cause respiratory distress, only the skin can be closed. Postsurgical complications include infection, erosion of the patch into adjacent tissues, chest wall deformity, restrictive lung disease, and recurrence. Approximately 7% of those who undergo primary repair often show recurrence within the first year. Prosthetic materials cannot grow with the patient, so this type of repair has a high probability of recurrence over time (up to 40%). The use of patches carries a high recurrence rate and may cause progressive chest wall deformity; it is recommended to perform repair with autologous tissues, such as a latissimus dorsi or rectus abdominis muscle flap or free fascia lata.[8] Some criteria can be considered to predict the prognosis before surgery. Blood pH <7, partial pressure of carbon dioxide >100 mmHg, stomach being present in the thorax, and pneumothorax development are poor prognostic indicators.[5]

MORGAGNI HERNIA

Description and etiology

On both sides of the sternum, there is a potential space called the foramen of Morgagni or the Larrey space, through which the internal mammary arteries pass and continue with the name of superior epigastric arteries. Morgagni hernia is a congenital defect caused by the failure of the sternal and costal elements of the diaphragmatic crus to develop. If it is on the left side of the sternocostal hiatus, it is called Larrey hernia, and if it is on the right side, it is called Morgagni hernia. If the opening is wide enough to cover both sides, it is called Morgagni-Larrey hernia.[25] Hernia formation is less common on the left side due to the pericardium. It constitutes 5% of CDHs. There is a wide opening in the septum transversum, which causes an anterolateral defect. The names parasternal hernia, retrosternal hernia, and subcostasternal hernia may also be used. This type of hernia is observed on the right in 80%, on the left in 8%, and bilaterally in 2%, and a hernia sac is found in 95% of cases.[5] The most common organs in the hernial sac are the omentum (92%), colon (58%), stomach (25%), small intestines (11%), and liver (4%), respectively.[17]

Clinic

Morgagni hernias are usually asymptomatic at birth and may not be diagnosed until adulthood. However, some patients may present with severe respiratory distress during infancy. Symptomatic patients may sense weak substernal pain and pressure. If incarceration or strangulation develops, they may also apply to the emergency room with severe pain.[18] Rarely, if the abdominal content opens into the pericardium, it may cause cardiac tamponade and death.[5] Morgagni hernias can coexist with other anomalies such as Down, Turner, or Noonan syndromes, pentalogy of Cantrell, pectus deformities, bowel malrotation, and genitourinary malformations, at rates ranging from 34 to 50%.[26]

Diagnosis

The first method is posteroanterior chest radiography. While it can be seen as a pericardial mass, it is also possible for the intestinal tract to be visible in the thorax. Thorax CT can be used to confirm the diagnosis. Computed tomography is specifically diagnostic for only omental herniations (Figure 2). If complete evaluation of the omental fatty tissue cannot be done with CT, thorax magnetic resonance imaging can be performed. Video thoracoscopy is also a relatively noninvasive method that provides a definitive diagnosis.

Treatment

There is a risk of incarceration and strangulation in Morgagni hernias; as in all hernia cases, the defect should be improved with surgery when the diagnosis is made.[18] However, if the patients have no symptoms, the content of the hernia is only omentum, and are older age, the following can be done. A transthoracic or transabdominal approach may be used. However, today the preferred approach is laparoscopic, but in cases where this is not possible, laparotomy can also be applied.[27] If the preoperative diagnosis is clear, the transabdominal approach may be easier since it has the advantage of evaluating the nutrition and functional status of the abdominal organs reduced in this way. Moreover, postoperative pain is less, and hospital stay is shorter. For abdominal intervention, one of the epigastric, median, right subcostal, or paramedian incisions can be used. If the hernia is bilateral, a median laparotomy approach is more appropriate. After reduction of the herniated organs, the hernia sac is usually removed. The defect is closed without excessive tension to prevent recurrence. While small defects are closed primary intention using nonabsorbable sutures, it may be necessary to use synthetic materials for large defects, such as prolene (polytetrafluoroethylene). The same procedure can be successfully performed in patients who have not been diagnosed preoperatively and who have undergone thoracotomy due to a mass. In recent years, successful hernia repairs have been reported using video thoracoscopic or laparoscopic

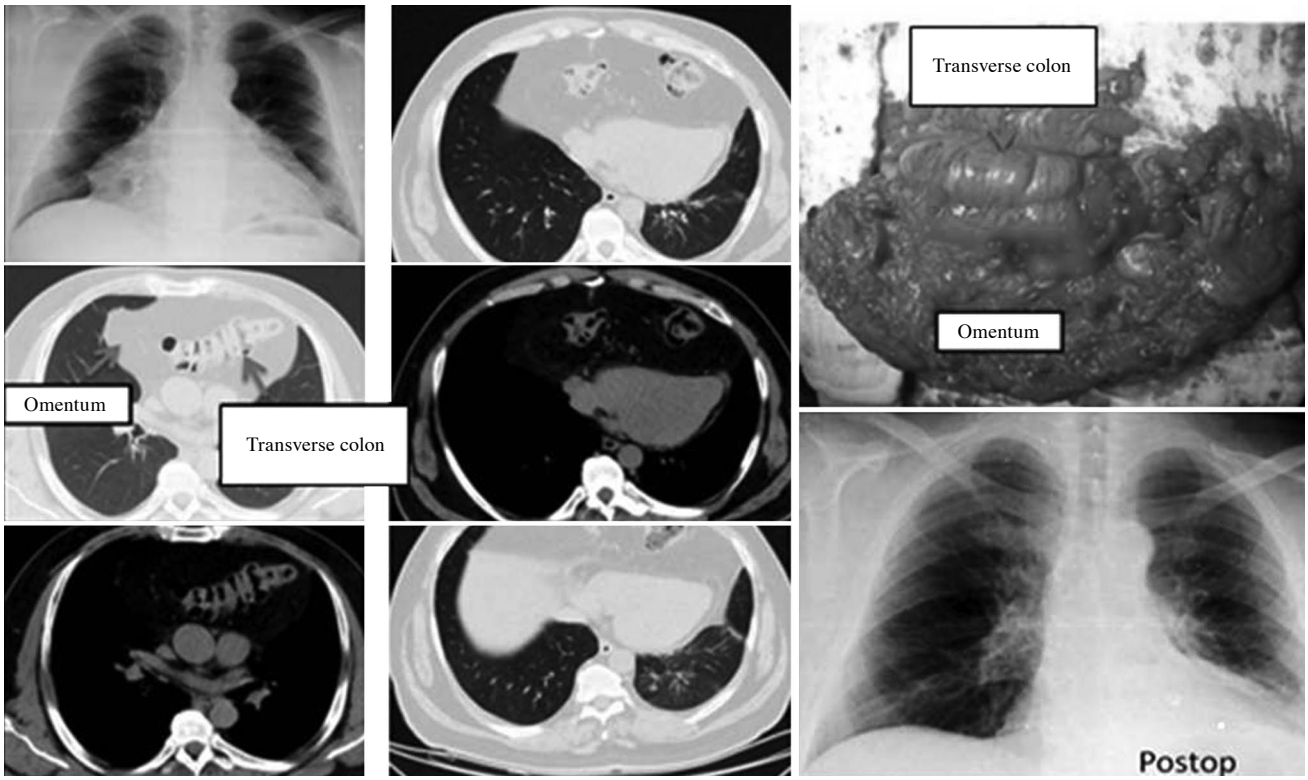

Figure 2. A case of Morgagni hernia encountered in adulthood.

approaches.[5] Recently, robotic series have also started to be published. However, these are mostly adult series. Although the patient stay is reduced in these series, the surgery time is longer than in the open series.[25]

Seven patients were operated on for Morgagni hernia in our clinic between January 2005 and June 2011. Four of the patients were female, and three were male. The mean age was 58.4±7.61 years (range, 52 to 74 years). Six patients had dyspnea, one patient had epigastric pain, and two patients had a history of traffic accidents. All patients underwent laparotomy. After the organs herniated into the thoracic cavity were reduced to the peritoneal cavity, the defect in the diaphragm was closed one by one with zero-number nonabsorbable sutures. In one patient, the hernia sac contained the colon and omentum, while in all other patients, the content of the hernia sac was the omentum. Defect sizes were as follows: the smallest was 5 cm, and the largest was 10 cm. All patients had a hernia on the right. Prolene mesh was used for hernia repair during the operation in two patients.

OTHER RARE DIAPHRAGMATIC HERNIAS SEEN IN CHILDREN

Intrapericardial diaphragmatic hernia

Definition and etiology

It is a very rare type of diaphragmatic hernia in which the abdominal organs herniate into the pericardium. It is also called peritoneopericardial hernia. This type of hernia is largely congenital in children and often traumatic in adults. It is thought to develop due to insufficient fusion of the pars sternalis of the septum transversum during diaphragm development.[28]

Clinic

Hernia may show itself as massive pericardial effusion or pericardial mass in the prenatal period. Most newborns show signs of severe respiratory distress and cyanosis due to pulmonary hypoplasia or massive pleural effusion in the early postnatal period.[29]

Treatment

Surgical repair is performed through the abdomen or thorax. Approach from the abdomen is often

preferred, and repair can be performed with minimally invasive techniques. The defect can be primarily sutured. However, in the presence of a defect that is too large to be closed primarily, the use of a musculofascial flap is recommended.[28]

Ventral diaphragmatic defect or central tendon defect

This type of defects occur in front of the inferior vena cava, at the level of both midclavicular lines. Ventral diaphragmatic hernia appears as a component of Cantrell's pentalogy. Anteromedial location of these hernias has also been reported.[30]

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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