Down Syndrome and Morgagni Hernia Association: A New Case and Review of the Literature

Down Sendromu ve Morgagni Hernisi Birlikteliği: Yeni Bir Olgu Nedeni ile Literatürün Gözden Geçirilmesi

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ABSTRACT Morgagni hernia is a well known congenital malformation seen with a frequency of 1/3000 newborns and often presents with little or no clinical signs and symptoms yet it could sometimes be associated with high mortality. Association of Morgagni hernia with several chromosomal and genetic syndromes is also well known however its association with Down syndrome is relatively rare. To the best of our knowledge up to date the literature reports 32 cases with Down Syndrome accompanied by Diaphragmatic (Morgagni) Hernia and those whose karyotype have been studied are stated to be regular Down syndrome patients presenting free trisomi 21, except one with t(21;21). Here we present the occurence of an asymptomatic Morgagni hernia in a thirteen month-old infant with a translocation type Down Syndrome {46,XY,der(13;21) (q10;q10),+21)}. There seems to be a co-existence between the occurence of Morgagni Hernia and trisomy 21 on the basis of embryonic connective tissue establishment. The relevant literature is discussed.

Key Words: Hernia, diaphragmatic; Down syndrome

ÖZET Morgagni hernisi yenidoğanda yaklaşık 1/3000 sıklıkla görülen ve iyi bilinen bir konjenital malformasyondur. Genelde asemptomatiktir ancak bazı olgular öksürük ve bazen de geçici kusmalarla başvurabilirler. Yakınmaların çoğu çok ağır olmayan klinik semptomlar olmakla birlikte, hastalık kimi zaman ölümle de sonuçlanabilir. Bu nedenle erken tanı ve tedavileri önemlidir. Literatür bilgileri, sıklıkla izole olarak ortaya çıkan bu malformasyonun, genetik sendromlara eşlik edebildiğini de göstermektedir. Morgagni hernisi ve Down sendromu birlikteliği oldukça enderdir. Bilgilerimiz ışığında literatürde toplam 32 olgu yer almaktadır. Bu olguların, karyotip çalışması yapıldığı bildirilenler arasında, bir olgu t(21;21) hariç, tümü klasik trisomi 21 genetik yapısına sahiptirler. Literatürde, embriyonik gelişim sürecinde rol alan diyafragma oluşum genleri, diyafragma gelişim defektleri ve Down sendromu ilişkisine dair veriler mevcuttur. Bu çalışmada 13 aylık bir translokasyon tip Down sendromlu bebekte {46,XY,der(13;21) (q10;q10),+21)} Morgagni hernisi birlikteliği aktarılmakta ve t(13;21) saptanan bu olgu nedeni ile literatür gözden geçirilmektedir.

Anahtar Kelimeler: Diyafragma hernisi; Down sendromu

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Down syndrome (DS) is a well known chromosomal disorder and is often associated with various organ malformations. Congenital heart diseases, renal abnormalities, central nervous system malformations, skeletal anomalies and gastrointestial system malformations are some of the conditions reported to accompany the syndrome. The association of Morgagni hernia with Down syndrome is however relatively ra-

re. Honoré et al., reported the presence of Morgagni hernia in 4.18% of infants with Down syndrome (California Birth Defects Monitoring Program).[1] Kava et al., reported from India, one child with Morgagni hernia in a large series of DS children (524 patients).[2]

Here we present the occurence of an asymptomatic Morgagni hernia in a thirteen month-old infant with Down syndrome who had an unbalanced Robertsonian translocation between chromosomes 13 and 21.

CASE REPORT

A13-month-old male infant was admitted to our genetic center via pediatric cardiology department where he was under investigation for a congenital heart abnormality. The patient was the second child of a 27-year-old mother. The parents were non-consanguineous. The first conception of the mother had resulted in a spontaneous abortion. The patient did have phototherapy during the newborn period due to hyperbilirubinemia. On physical examination he weighed 7750 g (3-10th percentile), he was 72 cm tall (3-10th percentile) and was microcephalic with a head circumference of 42.3 cm (<3rd percentile). The patient presented the classical stigmatas of Down syndrome. There were generalized hypotonia, micro-brachycephaly, flat facial features, protruding tongue, horizontal nystagmus, flat nasal bridge, bilateral epicanthal folds, upslanting palpebral fissures, small nose, small ear lobes, simian crease in the right hand, syndactyly between the second and third toes, and a gap between first and second toes. All his developmental milestones were delayed. He could sit without support but could not walk. No hypothyroidism was observed in the laboratory examinations. A translocation type Down Syndrome was detected via peripheral blood karyotype analysis: 46,XY,der(13;21)(q10;q10)+21. The parents were karyotyped and it was found out that the mother was the carrier of a balanced translocation for chromosomes 13 and 21: 45,XX,der(13;21)(q10;q10).

The echocardiographic examination revealed an atrial septal defect. An image mimicking a cystic adenomatoid malformation or a diaphragmatic hernia was detected in the chest radiograph (Figure 1). Computed tomography of the thorax could not make a clear distinction between a cyctic adenomatoid malformation or a Morgagni hernia. The radiographic examination after barium ingestion however, revealed herniation of the intestines into the thoracic cavity (Figure 2). Diagnosis of a Morgagni hernia was confirmed. The patient was operated and did well during the postoperative follow-up.

DISCUSSION

Congenital diaphragmatic hernia (CDH) occurs in approximately 1 in 3000 newborns and could sometimes be associated with a relatively high mortality. Different types of CDH exist including Bochdalek, Morgagni and and central (septum transversum) diaphragmatic hernia.[3]

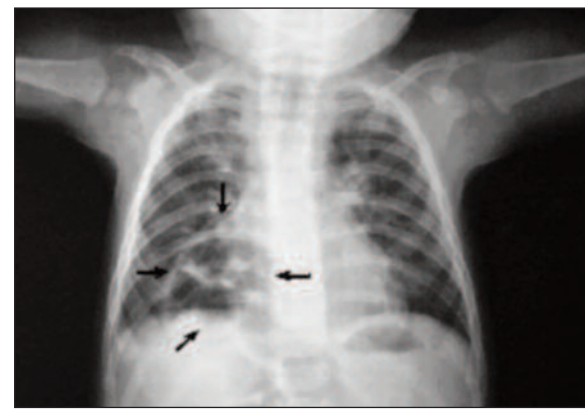

FIGURE 1: Plain chest radiograph showing air-filled cystic lesions at the right paracardiac area.

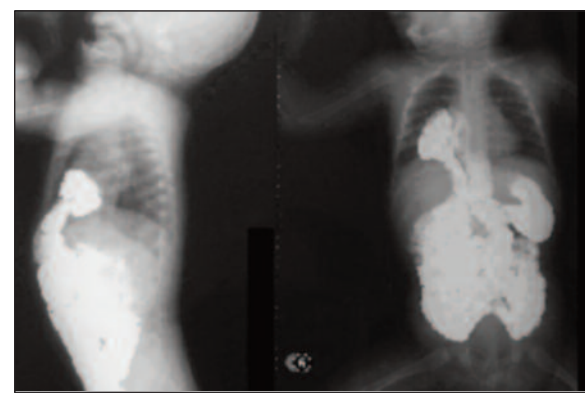

FIGURE 2: Barium study showing barium-filled loops of transvers colon herniating into the chest (lateral, -left and anterior, -right views).

Morgagni hernia (MH) is the least common of congenital diaphragmatic hernias. It accounts for only 1.5 to 5 % of the congenital diaphragmatic hernias.[4,5] Over a period of 25 years Pokorny et al., reported 4 cases of MH versus 74 infants with posterolateral (Bochdalek) hernias.[6]

Morgagni hernia forms in the anterior retrosternal diaphragm. It is suggested to be caused by the insufficient fusion of the fibrotendinous section of pars tendinous which stems from costochondral arch and fibrotendinous section of pars sternalis.[7] This cavity is usually filled with fat. It is covered with pleura in the upper part and with peritoneum in the lower part. Morgagni Hernia is seen in the anteromedial part where chest wall septum transversum meet. Most of it is located in the right hemithorax (90%), eight percent is located on the left and two percent is bilateral. Most frequently there is large intestine, liver, omentum and stomach in the sac.

The pathogenesis and etyology of CDH is not elucidated yet. Teratogen induced mice models suggest that the defects of diaphragmatic muscle arise from maldevelopment of the primordial diaphragm, the pleuroperitoneal fold.[8] The conributi-on of connective tissue to the development of the diaphragm is unknown. Recently a study established the identification of the role for Slit3 gene in regulating the development of the fetal diaphragm.[9]

MH usually presents late in childhood and shows minimal or no symptoms. It is often discovered incidentally during the evaluation of other non-related symptoms. Rarely it is seen in the neonatal period and in infants with respiratory distress and cyanosis. Symptoms are coughing, vomiting after meals, constipation, diarrhea, postprandial fullness and respiratory tract infections.[1-10] Some cases of infancy are accidentally identified by the appearance of air liquid levels and solid masses in the chest radiograph.

Morgagni hernia mostly appears to be an isolated congenital defect however association with childhood congenital heart defects such as ventricular and atrial septal defects, patent ductus arteriosus, tricuspid valve failure, tetralogy of Fallot, anomalous pulmonary venous return and endocardial cushion defect, is reported.[7] Omphalocele, retroperitoneal teratoma, and genitourinary anomalies also accompany the Morgagni hernia. The defect can as well occur in association with some genetic syndromes. Turner syndrome, Prader Willi syndrome, Thoraco-Abdominal syndrome (Cantrell's syndrome), Noonan syndrome are some of them. Association of MH with some chromosomal defects[11-13] is occasionally reported. Its occurence with Down syndrome is however relatively rare.[1-2] Pokorny et al., in a series of 22 infants with MH reported association with DS in 3 cases (14%).[6] A more recent review by Kubiak et al., on the other hand raised this incidence to 34.8%.[14]

To the best of our knowledge the literature review revealed 32 cases with Down syndrome accompanied by Diaphragmatic (Morgagni) hernia (Table 1). The age of diagnosis of these cases ranged from neonatal period to 37 years of age. The cases karyotyped were all classical trisomy 21 except the case of Kubiak et al., and ours (Table 1).[14] The most common symptoms were recurrent respiratory tract infections, coughing, and vomiting especially after feeding, however it could be asymptomatic as it was in our case. There seems to be a relationship between the occurence of Morgagni hernia and trisomy 21. The migration of rhabdomyoblasts from paraxial myotomes to the defective dorsoventral area as a result of increased cellular adhesion is suggested to have an impact on this co-existence.[1] It is well known that children with DS have other muscular defects such as ventral hernia and diastasis recti, umblical hernia, and a general muscular hypotonia. Most of the associated congenital heart defects are also of muscular type. This association as well as that with MH may suggest a possible role of a common muscular deficiency in DS patients. Slit proteins are suggeted to be participating in the formation and maintenance of the nervous and endocrine systems by protein-protein interactions as they are shown to be functioning as guidance cues for myoblasts as well as motor axons, olfac-

TABLE 1: Trisomy 21 and Morgagni Hernia (Literature Review) - 32 cases.

Case no.	Author	Age/Sex (M/F)	Clinical findings	Karyotype
1	Kotobi et al., 2005	11 year-old (F)	Abdominal pain, vomiting gastric volvulus,	No data
2	Kava et al., 2004	?	Duodenal Atresia	Trisomy 21
3	Naveed-ur-Rehman et al., 2004[22]	1 year-old (M)	Recurrent chest infections, fever, hypothyroidism	No data Clinical stigmata of DS
4	Ceylan et al., 2004[23]	37 year-old (F)	Abdominal pain, nausea, vomiting	No data
5,6,7	Al –Salem et al., 2002	8 year-old (M), 9 month-old (M), 13 month- old (F)	Recurrent respiratory infections, respiratory distress	No data
8	Parmar et al., 2001	12 month-old (M)	Recurrent respiratory distress, chest deformity.	47,XY,+21
9	Kubiak et al., 1998	4 ½ year-old (M)	Vomiting, fever, thorax deformity	46,XY,t(21; 21)
10	Latif Al-Arfaj A., 1998[24]	9 month-old (M)	Respiratory distress, pulmonary infection	Trisomy 21
11	Becmeur et al., 1998[25]	11 year-old (M)	?	No Data
12	Quah and Menon., 1996	5 month-old (M)	Retroperitoneal teratoma	Trisomy 21
13,14,15	Honoré et al., 1993	3 newborns	Registry record data	Trisomy 21 (all 3 cases)
16, 17	Harris et al., 1993	Twins	?	Trisomy 21 (all 2 cases)
18,19,20	Elawad ME., 1989[26]	15 month-old (m), 1 year-old (m), 8 month-old (m)	*Recurrent respiratory infections, *Chest deformity, RVH *Respiratory distress, ASD-RVH *Pulmonary infection	Trisomy 21 (all 3 cases)
21,22,23	Berman et al.,1989[27]	?	No symptoms	Trisomy 21 (all 3 cases)
24,25,26	Pokorny et ai., 1984	All 3, infants	Respiratory distress; 2 cases had as well "omphalocele"	Trisomy 21 (all 3 cases)
27	Thomas and Clitherow, 1977[28]	?	?	Trisomy 21
28,29,30,31	Salzstein et al., 1951[29]	?	?	Trisomy 21 (all 4 cases)

tory bulb axons, neuronal cells, and leukocytes.[15,16] Thus somehow they might be contributing to these arguments. Recently a genetic model for the development of a central (septum transversum) congenital diaphragmatic hernia in mice lacking Slit3 has been described.[9] Furthermore the DNA regulatory proteins, myocyte-specific enhancer factor 2 proteins (MEF2), are suggested to play a critical role in the control of muscle differentiation and diaphragmatic formation.[12]

Although MH is known to be a rare congenital disorder, a surprisingly high incidence is reported from Saudi Arabia.[17] The reason for this high incidence is not clear. Due to the fact that MH is associated with DS and is reported in identical twins it is suggested it to be an inherited disorder.[17,18] The high rate of consanguinity in the relevant region is presumed to contribute genetically to the increased incidence of MH. Possible impact of an autosomal recessive inheritance have occasionally been described in MH.[2-19,20]

Similar to other literature reviews our case also emphasizes the need for research of diaphragmatic hernias as a possible cause of respiratory distress in DS patients. As the mode of presentation of hernia is variable increased awareness of physicians is needed. If the lung x-ray raises doubts about hernia the diagnose should be confirmed with ultrasonography, computerised tomographic scans or barium ingestion studies. The hernias are operated because incarceration and strangulation may occur in delayed cases.[21]

Increased incidence of association of DS with MH in recent reports might even raise the suggestion of screening asymptomatic DS cases for a possible association with MH at least in regions with a high consanguinity rate as there seems to be a possibility of increased incidence in such localizations.

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