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Case Report

Co-existence of Two Rare Conditions: Oculo-Palato-Cerebral Syndrome and Congenital Chylothorax

Seyhan Erisir Oygucu[1*], Gonul Tezel[2], Muhammet Kazim Erol[3], Ozgur Erkal[4]

1. Division of Neonatology, Department of Pediatrics, Faculty of Medicine, University of Kyrenia, Kyrenia, North Cyprus
2. Division of Neonatology, Department of Pediatrics, Antalya Training and Research Hospital, Antalya, Turkey
3. Department of Ophthalmology, Antalya Training and Research Hospital, Antalya, Turkey
4. Division of Medical Genetics, Department of Pediatrics, Antalya Training and Research Hospital, Antalya, Turkey

ABSTRACT

Background: Oculo-palato-cerebral syndrome is an extremely rare condition characterized by various features, including low-birth weight, microcephaly, cerebral atrophy, mild-to-severe developmental delay, cleft palate, persistent hyperplastic primary vitreous, microphthalmia, small hands and feet, joint laxity, and large ears with thick helices. Diagnosis of this syndrome is based on the clinical manifestations, particularly the presence of persistent hyperplastic primary vitreous in association with other malformations. Congenital chylothorax is also a rare condition in the neonatal period, which is caused by the abnormal accumulation of the lymphatic fluid within the pleural space. This condition may be detected prenatally or during the neonatal period.

Case report: We presented the case of a patient with oculo-palato-cerebral syndrome and congenital chylothorax based on a literature review.

Conclusion: Oculo-palato-cerebral syndrome and congenital chylothorax are both rare conditions. To the best of our knowledge, this was the first case report on congenital chylothorax in association with oculo-palato-cerebral syndrome in the available literature. Since there have only been five case reports on these patients, further evidence is required to confirm the possible association between these rare conditions.

Keywords: Congenital chylothorax, Oculo-palato-cerebral syndrome, Persistent hyperplastic primary vitreous

Introduction

Congenital chylothorax (CC) is defined as the abnormal accumulation of the lymphatic fluid within the pleural space, which may be detected prenatally or during the neonatal period. CC is caused by multiple lymphatic vessel anomalies or thoracic cavity defects and may accompany other congenital anomalies (1). The incidence of CC is estimated to be one case per 8600-10,000 live births. It is considered to be the most common cause of pleural effusions in the neonatal period (2, 3). Moreover, CC may be associated with chromosomal abnormalities and various conditions, such as Turner, Noonan, and Down syndromes (4, 5).

Oculo-palato-cerebral syndrome is an extremely rare condition, which was first described by Frydman et al. (6). It is characterized by the combination of low birth weight, microcephaly, persistent hyperplastic primary vitreous (PHPV), microphthalmia, full cheeks, large ears with thick helices, cleft palate, small hands and feet, joint laxity, hearing loss, mild-to-severe developmental delay, and cerebral atrophy. Diagnosis of this syndrome is based on the clinical manifestations, particularly the presence of PHPV in association with other malformations. Oculo-palato-cerebral syndrome is supposed to be inherited in an autosomal recessive pattern; however, the causative gene or locus has not yet been identified (6, 7).

In this study, we presented the case of a patient with oculo-palato-cerebral syndrome and

* *Corresponding author:* Seyhan Erisir Oygucu, Division of Neonatology, Department of Pediatrics, Faculty of Medicine, University of Kyrenia, Sehit Yahya Bakır Sokak, Karakum, Kyrenia, North Cyprus. Tel: +903924449939, 05338459909; Fax: +903926502686; Email: seoygucu@hotmail.com

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unilateral CC.

Case report

A male neonate was born with the gestational age of 33 weeks, and his prenatal anthropometrical measurements were compatible with 26 weeks of gestation. The infant was delivered via cesarean section due to maternal preeclampsia, polyhydramnios, and fetal distress. He was the fourth live-born child of a third-degree consanguineous Turkish couple. The father had a brother who was said to have cognitive disability and deceased during childhood; unfortunately, the family had no medical records of him. Prenatal ultrasonography at week 29 of gestation showed microcephaly and intrauterine growth retardation in the fetus.

The one- and five-minute Apgar scores of the neonate were 5 and 7, respectively. His birth weight was 1180 grams (<3rd percentile), with the length of 38 centimeters (<3rd percentile) and head circumference of 25 centimeters (<3rd percentile). Physical examination revealed microcephaly, bulbous nasal tip, cleft palate, full cheeks, microretrognathia, large ears, right undescended testis, and respiratory distress symptoms (tachypnea, grunting, and retractions) in the neonate.

The infant was intubated and received mechanical ventilation. His chest radiograph showed the signs of respiratory distress syndrome, and the patient received a dose of surfactant. His control chest radiograph revealed right-sided pleural effusion in the hemithorax (Figure 1). In addition, thoracic ultrasonography showed massive pleural effusion, and a chest drain was attached to the right side of the neonate. The pleural fluid was clear, total cell count was 600/ml with 60% lymphocyte fraction, triglyceride was 32 mg/dl, protein was 3.3 g/dl (pleural fluid-to-serum protein ratio: 0.75), lactate dehydrogenase (LDH) was 333 mg/dl (pleural fluid-to-serum ratio: 0.71), and albumin gradient was 0.5. According to Light's criteria, the fluid was identified as an exudate (8). Serological tests for toxoplasma, rubella, cytomegalovirus, and parvovirus B19 were negative. In addition, echocardiography showed clinically insignificant ventricular septal defects with normal cardiac dynamics.

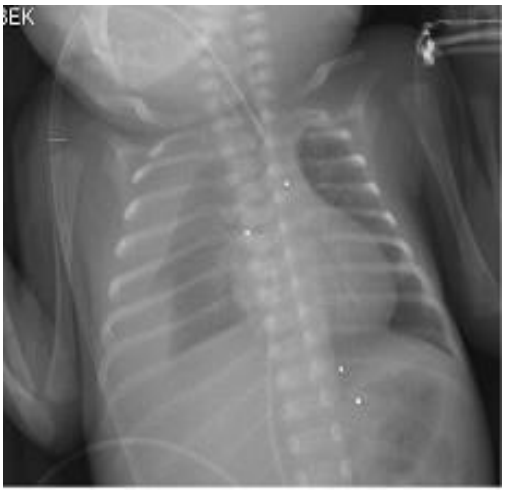

Figure 1. Chest Radiograph after Surfactant Administration Showing Severe Right-sided Pleural Effusion

Total parenteral nutrition was initiated on day one of birth, and minimal enteral feeding was started on day four of birth. Chest X-ray and ultrasound showed no pleural effusion on day 15 of birth, and the drain was removed. The neonate was extubated and attached to nasal continuous positive airway pressure. On day 27, he received full enteral feeding; however, his respiratory status deteriorated, and the patient was reintubated. A chest drain was also attached to the neonate since chest X-ray and thoracic ultrasonography revealed right-sided pleural effusion in the hemithorax. The pleural fluid was turbid, and triglyceride level was 276 mg/dl. Enteral feeding was rearranged with a medium-chain triglyceride (MCT)-supplemented formula (Pepti-Junior, Aptamil, Apta Nutrition, Australia) in order to decrease the flow of chyle from the intestinal tract. The respiratory condition of the neonate improved gradually, and no pleural fluid re-accumulation was observed in thoracic ultrasonography on day 41 of birth. As a result, the patient was extubated, and the chest drain was removed as well. After the removal of the chest tube, no pleural effusion re-accumulation was detected.

Cranial ultrasound showed the dilation of the lateral and third ventricles and hydrocephalus with the ventriculo-cephalic index of 45%. Magnetic resonance imaging of the brain demonstrated the dilation of the lateral and third ventricles, as well as bilateral cerebral atrophy. In the ophthalmological examination, the right eye of the infant was micro-ophthalmic, a bilateral cataract was observed in the lenses, and optic atrophy was present in the left eye. Moreover, the fundus of the left eye had a salt and pepper appearance with diffuse microhemorrhages. No retinopathy of prematurity was detected, while an avascular area was observed in zone two.

Figure 2a-2b. Patient on Day 60 (note microcephaly, bulbous nose, full cheeks, large ears with thick helices, microretrognathia, and microphthalmia of right eye)

Additionally, the cornea of the right eye was small and clear, while the fundus was not visible due to the cataract. A cone-shaped retrolental echogenicity was revealed in the ocular ultrasonography of the micro-ophthalmic right eye of the patient. Combined PHPV was diagnosed by an ophthalmologist, and peripheral chromosome analysis revealed normal male karyotype (figures 2a & 2b).

In week 43 of the corrected gestational age, the neonate still had feeding problems due to cleft palate and cricopharyngeal incoordination. As such, laparoscopic gastrostomy was performed, and the patient was discharged two weeks later on full enteral feeding via a gastric tube. Informed consent was obtained from the family of the infant.

Discussion

Oculo-palato-cerebral syndrome is a very rare condition, which was first described by Frydman et al. (6) in 1985 in three Moroccan, Jewish children of consanguineous parents. The fourth case was reported by Pellegrino et al. in 2001 (9), which was an infant born to a non-consanguineous couple of Eastern European, Jewish descent. Three years later, Alanay et al. (7) reported the case of a child born to a Turkish, first-degree cousin couple, supporting the autosomal recessive inheritance of the syndrome.

In this study, we have presented the sixth case of oculo-palato-cerebral-syndrome in the available literature. Similar to the previous cases, our patient had a history of maternal hypertension and intrauterine growth retardation.

In addition to unilateral PHPV, right microphthalmia, bulbous nose, large ears with thickened helices, cleft palate, cryptorchidism, microcephaly, and diffuse cerebral atrophy, our patient was also born with unilateral CC, which is distinctive compared to the previously reported cases. CC is the most common etiology of neonatal pleural effusions (2, 10) with the male-to-female ratio of 2:1. CC commonly occurs bilaterally; however, if the collection is unilateral, right-sided collection is relatively more common (11-13). In the present study, the patient was male with right-sided collection.

Accumulation of chyle in the pleural space is resulted from thoracic or lymphatic anomalies. Thoracic lymphangiomas, primary pulmonary lymphangiectasis, congenital lymphangiomatosis, and congenital lymphatic dysplasia syndrome may be the underlying pathologies of CC in the neonatal period (14). CC also occurs in association with dysmorphic syndromes, such as Noonan syndrome, Turner syndrome, and trisomy 21, which are the most commonly associated syndromes with CC (4, 5). According to the previous studies in this regard, CC has been associated with Alagille syndrome, chromosome 13 translocation, and 47 XYY and 47 XXX/46 XX mosaicism (13, 15). To the best of our knowledge, this was the first case report on CC in association with oculo-palato-cerebral syndrome.

The nature of a pleural effusion is identified based on the physical appearance, cell count, and triglyceride, serum and pleural fluid LDH, protein, and albumin levels. In our patient, the initial pleural fluid was clear, triglyceride level was low,

and white blood cell count was <1,000, with less than 70% of the cells presenting as lymphocytes compatible with exudate according to Light's criteria (8). Since exudates result from increased capillary permeability or lymphatic leakage, even if the initial characteristics are not compatible with CC (as in our patient), exudates should be followed-up closely after the initiation of enteral feeding. After full enteral feeding with a turbid nature, the high triglyceride level of the pleural fluid confirmed the diagnosis of CC, and the management strategy changed accordingly.

Management of CC may be conservative or surgical. Conservative management aims to reduce chyle production and control the symptoms by draining the chylous effusion from the chest cavity. In the cases with large volumes of effusion that compromise respiration, the initial step in the management of the condition should involve inserting a chest tube for diagnostic purposes, as well as the drainage of the pleural space in order to allow the re-expansion of the lung. This may tamponade the duct or lymphatic defect, allowing the spontaneous closure of the lymphatic vessels or developing adequate collateral connections (2, 16). Daily drainage volume is used by some care centers as a guideline for clinical improvement or failure (10 ml/kg/day of pleural drainage is considered an improvement, and 10 m/kg/day of pleural drainage is considered a failure after four weeks of nonsurgical management) (17).

In order to decrease the lymphatic flow, a successful management strategy for CC in newborns involves the cessation of enteral feeding and initiating total parenteral nutrition for a period, followed by a formula containing MCT, which bypasses the intestinal lymphatic system and is directly absorbed to the portal vein (18). Octreotide, which is a synthetic somatostatin analog, may also be used for the treatment of CC in neonates (19-21). This approach has been shown to be effective through reducing the lymphatic fluid production and lymphatic flow in the thoracic duct (22, 23). A Cochrane review on the role of octreotide in neonates was published in 2010, reporting insufficient data to support its routine use for this condition and recommending a large multicentre trial in this regard (24). In the cases of refractory effusions, surgical interventions, pleurodesis or the placement of a pleuroperitoneal shunt may be performed (16).

In our patient, a chest tube was inserted for drainage due to respiratory distress and massive pleural effusion in the infant. On day 15, the findings of pleural effusion resolved, and the drain was removed. When the pleural fluid was re-accumulated with signs of significant respiratory distress, the chest tube was re-inserted, and the fluid was re-evaluated compatible with chyle. Non-surgical treatment has proven successful in more than 80% of the cases in the previous studies. However, the response to medical therapies may take weeks in the patients with CC (17, 25). The response of our patient to conservative therapy was fairly prompt. After the cessation of enteral feeding, total parenteral nutrition and dietary modification with an MCT-supplemented formula caused CC to subside in the patient within 14 days. Therefore, further therapeutic interventions were not required.

In conclusion, oculo-palato-cerebral syndrome and CC are both rare conditions. To the best of our knowledge, this was the first case report on CC in association with oculo-palato-cerebral syndrome in the available online literature. Since there have only been five reported cases in the previous studies, further evidence is required to confirm the possible association of these rare syndromes.

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Conflicts of interests

None declared.

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