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CASE REPORT

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Escobar syndrome: non-lethal multiple pterygium syndrome case report

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Abstract
Escobar syndrome is a rare disorder that is a nonlethal variant of multiple pterygium syndromes. It is usually diagnosed in utero on fetal ultrasound and then confirmed in the neonatal period. Escobar syndrome is characterized by arthrogryposis multiplex congenita, excessive pterygia, congenital contractures, and abnormal facial appearance. It manifests as an autosomal recessive condition, and is caused by homozygous or compound heterozygous mutation of the CHRNG gene. Other variable features include growth retardation, congenital respiratory distress, ptosis, low set ears, cleft palate, and cryptorchidism. In this article, a newborn patient with Escobar syndrome was presented to share difficulties in the neonatal period, and the clinical features were discussed in the light of the literatüre.

Keywords: Arthrogryposis, Escobar, multiple pterygium syndrome, newborn

Introduction

Escobar syndrome is a rather rare syndrome occurring with mutation in CHRNG gene and the inheritance is autosomal recessive. Skeletal systems anomalies such as pterygia in major joints, arthrogryposis, and rocker-bottom feet constitute its main clinical characteristics. In addition, head, neck, genitourinary system, abdominal wall and chest wall anomalies and short stature are common.

In the neonatal period, respiration problems occur in these infants due to different causes. In this article, an Escobar syndrome diagnosed case requiring mechanical ventilation due to respiratory problem and had diaphragm eventration was presented to share the difficulties experienced and the related literature was examined.

Case Presentation

Baby girl was delivered by cesarean section at 38th week from the first pregnancy of a 23 years old mother. Apgar scores were 5 and 7 at 1st and 5th minutes of life respectively. The patient who had postnatal respiratory problem was hospitalized in neonatal intensive care unit. Skeletal anomalies, bilateral rocker bottom feet, and polyhydramnios were present in prenatal story. Respiratory support, antibiotics treatment and total parenteral nutrition were started.

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The infant's birth weight was 2540 g (10-50p), length was 37 cm (<10p) and head circumference was 35 cm (50-90p) in the physical examination. Pterygia were present in the neck, axillary, antecubital and popliteal areas and arthrogryposis was present in these joints (Figure 1). The patient with micrognathia had a short neck and low-located ears (Figure 2). Flexion contracture and movement restriction were present in wrist and fingers (Figure 3). Rocker-bottom appearance was present in both feet (Figure 4). The decrease in respiratory sounds and tachypnea were present. There was no significance in other system inspections.

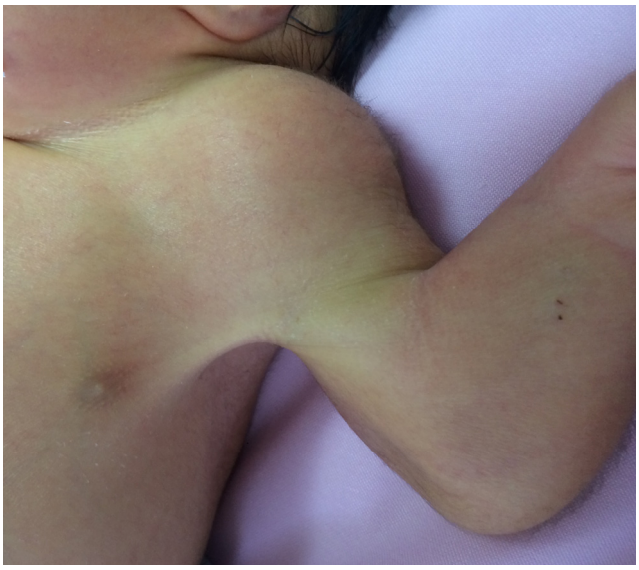

Figure 1. Defining pterygia in the neck, axillary, antecubital joints and short neck

Again no significance was found in total blood count and biochemical examinations. Lung hypoplasia and diaphragm eventration on the right side were observed on the roentgenogram (Figure 5). No dysplasia findings were found on skeletal graphics. Secundum ASD was detected in echocardiography. Abdominal ultrasonography was evaluated as normal. No pathologies were found for 13, 18, 21, X and Y-chromosomes in the chromosome inspection made and karyotype was XY. No pathologies were found in the cranial MR taken.

Figure 2. Defining micrognathia, short neck, and low-located ears

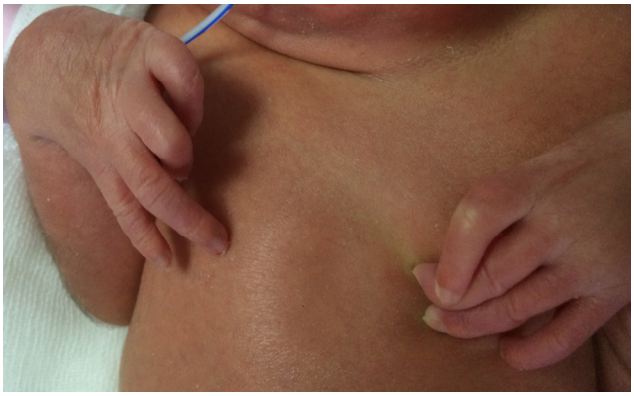

Figure 3. Defining hand characteristic

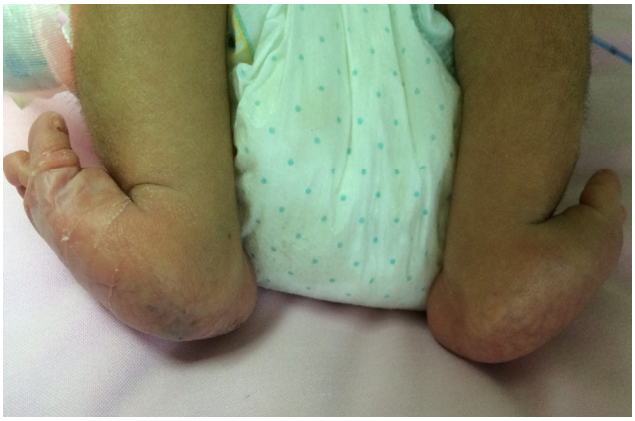

Figure 4. Defining rocker-bottom feet

With these findings, it was considered that the patient could have Escobar Variant Multiple Pterygium Syndrome (EVMPS). But no advanced investigation was made for CHRNG gene. The patient had respiratory support with ventilator for nine days in total including three days of intubation during the patient monitoring period. Enteral feeding with orogastric tube was started on the second day and complete enteral feeding was started on the tenth day. But the patient couldn't tolerate oral feeding and anti-reflux treatment was also started and enteral feeding with orogastric tube was continued

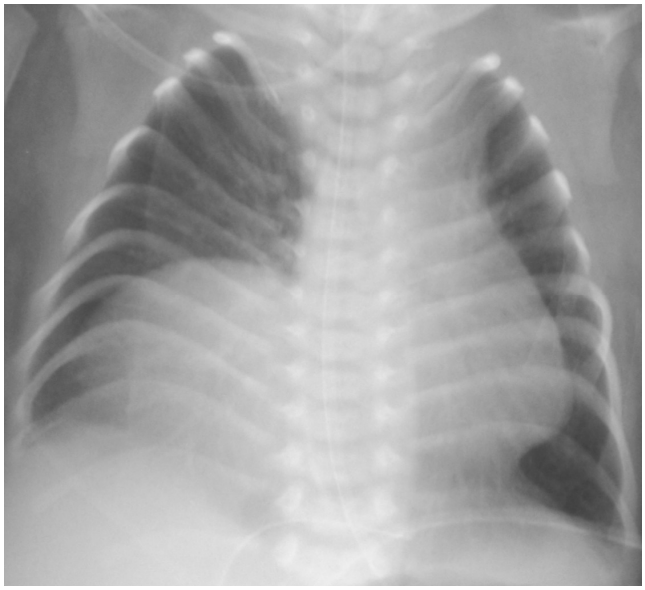

Figure 5. Defining diaphragm eventration on the right

Orthopedics, physical therapy and neurology departments evaluated the patient. An operation for freeing the joints was planned for the future for the patient who was taken in physical treatment program. The patient was in a positive general condition and was discharged on the 30th day with outpatient follow-up. The patient came for her last follow-up when she was three months old and it was observed that she continued physical treatment and started oral feeding. Her length, weight, and head circumference were below third percentile.

Discussion

Multiple Pterygium Syndrome (MPS) is diagnosed early with pterygia (skin remains combining proximal and distal of the joints, web) located in axillary, antecubital, popliteal areas and many joint areas such as neck, flexion contractures of these joints, intrauterine growth deficiency and other accompanying anomalies [1]. In clinic terms, it has two variants; lethal MPS and non-lethal Escobar variant.

Most of the patients have mutation in CHRNG located on the long branch of the second chromosome [2]. CHRNG gene encodes the gamma subunit of the acetylcholine receptors. Acetylcholine receptors becoming defective due

to the mutation in this gene also prevent neuromuscular transfer and fetal akinesia deformation occurs. A clinical variant of the disease changes according to the severity of the mutation and expression time of the gene. The inheritance is autosomal recessive and is equal in both genders but the prevalence is unknown [3]. Apart from this, the mutations in CHRNA1 and CHRND genes were reported to be LMPS related [4]. Autosomal dominant and X-related inheritances were also reported. In our case, lack of consanguineous marriage and familial pterygium-characterized case made us consider that the case could be sporadic. Sporadic Escobar syndrome cases were also defined in literature [5]. But parents from the same village, the narrowness of gene pool and miscarriages of nieces and nephews married makes us consider recessive inheritance.

The lethal form usually leads to fetal or early neonatal death. In the postmortem examination of patients with lethal MPS diagnosis, hypoplasia in vital organs such as lung, heart and brain and anomalies in urinary and gastrointestinal systems were reported [6].

Apart from multiple pterygia, short stature, micrognathia, long face, low-set ears, hypertelorism, lung hypoplasia, genitourinary anomalies, hand and foot anomalies can be named among the clinical characteristics of the non-lethal form known as Escobar syndrome. Non-lethal MPS syndrome was diagnosed clinically in our patient due to the presence of multiple pterygia, joint contractures, hand and foot anomalies and near fatal anomaly.

Intelligence is unaffected in Escobar syndrome but muscular-skeletal system related morbidities constitute a significant problem. A multidisciplinary approach with a team including a pediatric orthopedist, neurologist, physiotherapist, and neonatologist are required for patient management. The most significant problems in the neonatal period are respiratory problems and nutrition difficulties. Respiratory problems can both be related to RDS in premature newborns and pulmonary hypoplasia or diaphragm hernia. Respiratory problem due to diaphragm eventration on the right side and related lung hypoplasia was present in our patient, too. A significant problem is the intubation of these patients [2]. Intubation is unsuccessful due to short neck and pterygia in the neck most of the time and fiberoptic bronchoscopy use may be required. Laryngeal mask and inhaler anesthetics may be used for operation [7]. Although there were difficulties in intubation due to anatomic restrictions in our patient, oral intubation was successful.

Nutrition problems such as oral feeding intolerance and gastroesophageal reflux starting in early period and regressing later were reported in some patients [8]. These findings were observed in our patient and medical anti-reflux treatment was started. Anti-reflux treatment was partially useful. It was observed that the patient who was discharged with OGS tolerated oral nutrition well in the third month. Nutrition problems in these patients were considered to be related to anatomic restrictions such as pterygia restricting neck movements, short neck, and micrognathia. Also, hypotonia and swallowing dysfunction occurring due to neuromuscular transfer decreased due to the defect in acetylcholine receptors in these patients cause polyhydramnios by contributing to this situation [8]. Prenatal polyhydramnios was detected in our patient. Michalk et al reported that they had to place percutaneous endoscopic gastrostomy tube due to nutrition problems in two patients in their article on acetylcholine receptor pathway mutation-related fetal akinesia patients [9].

Short stature and growth deficiency are observed in more than 1/3 of these patients later. Starting from early period, they should be followed-up by an expert for nutrition support.

Physiotherapy, traction exercises and, if required, release surgery should be made in early period so that the joints may gain their functions. There is no suggested operation timing and it should be decided individually. Positive results of physical treatment and rehabilitation applications are reported [10]. Reporting that surgery demanding scoliosis may develop at advanced ages, if not in the early period and thus patient follow-up is recommended.

Result

MPS diagnosis should be considered in infants with prenatal or postnatal pterygium in neck and joints and genetic consultation service should be provided to the family. In patients without non-lethal anomaly and for whom EVMPS is considered, attention should be paid to respiratory and nutrition problems in the neonatal period and physical treatment and rehabilitation practices should be started at the early period.

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