



Conjugated Hyperbilirubinemia in a Neonate with Meconium Ileus and Congenital Hypothyroidism

Mekonyum İleus ve Konjenital Hipotroidizm Olan Bir Yenidoğanda Konjuge Hiperbilirubinemi

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SUMMARY

Meconium ileus is a unique manifestation of cystic fibrosis. Different anomalies associated with meconium ileus, consequently in cystic fibrosis, were reported but our case was the first reported with congenital hypothyroidism demonstrating significant conjugated hyperbilirubinemia. There are detailed explanations about the mechanisms of these two entities but we found no possible common pathway for these diseases in the evaluation of the literature. We suggest that this unique formation may only be coexistence. Congenital hypothyroidism may be evaluated for the patients with cystic fibrosis when conjugated hyperbilirubinemia is detected.

Key Words: *Meconium ileus, conjugated hyperbilirubinemia, children, cystic fibrosis.*

ÖZET

Mekonyum ileusu kistik fibrozisin eşsiz belirtisidir. Mekonyum ileus ile çeşitli birliktelikler, özellikle kistik fibrozis rapor edilmiştir; ancak hastamız kistik fibrozis ile beraber rapor edilen ve konjenital hipotroidizm ile konjuge hiperbilirubinemi bulunduran ilk hastadır. Bu iki durumun mekanizmaları için detaylı açıklamalar bulunmaktadır; ancak literatür araştırması sonrasında muhtemel ortak mekanizma için bir açıklama bulunamamıştır. Bu durumun sadece birliktelik olduğu düşünülmüştür. Konjenital hipotroidizm kistik fibrozis olan ve konjuge hiperbilirubinemi olan hastalarda göz ardı edilmemeli ve araştırılmalıdır.

Anahtar Kelimeler: *Mekonyum ileus, konjuge hiperbilirubinemi, çocuk, kistik fibrozis.*

INTRODUCTION

Meconium ileus (MI) is caused by sticky and inspissated intraluminal meconium based on intestinal and pancreatic dysfunction (1). MI is unique to CF (2). It is the earliest clinical manifestation of the cystic fibrosis (CF) and occurs in 10% to 20% of the neonates (3). Some associations with CF were determined like jejunoileal atresia, gallbladder disease, gastroesophageal reflux disease, lung disease especially in the right upper lobe, bronchiectasis, pulmonary bleb formation, rectal prolapse and inguinal hernia (4).

Congenital hypothyroidism (CH) has not been reported with CF although it is the most frequent endocrine disease that occurs in the early phases of life (5). Cardiac anomalies were reported with CH like atrial septal defect, tetralogy of Fallot, and pulmonary stenosis (6). Also associations with kidneys, lungs, brain and with some organs were described (7).

To our knowledge, our patient is the first with meconium ileus and congenital hypothyroidism, therefore, we aimed to report this association.

CASE REPORT

Three days old female patient suffering from intestinal obstruction was admitted to our neonatal intensive care unite. She had not passed meconium in three days time and had begun biliary vomiting. In physical examination, she was moderately dehydrated and had severe abdominal distention. Other physical examinations were seemed to be normal. There was gas distention located at upper abdomen in abdominal plain x-ray evaluation and total bilirubin level was 8.32 mg/dL and conjugated bilirubin was 0.5 mg/dL in laboratory findings. Sweat test resulted as 68 mmol/L. Other laboratory findings were normal. Barium enema revealed unused colon. The patient was operated for intestinal obstruction etiology. Sevoflurane 8%, 1 µg/kg fentanyl and 1 mg/kg vecuronium bromide was used for anesthesia induction. For anesthesia maintenance sevoflurane 2% and 50/50% air/O₂ mixture were used. Fentanyl was added if needed. In explorative laparotomy, dilated terminal ileum containing viscous and large amount of gait was detected. MI was diagnosed and high level divergent jejunostomy was performed. Midazolam and fentanyl was used for analgesia in the postoperative first day. In the second postoperative day, total and conjugated bilirubin levels were found to be 20.94 mg/dL and 5.54 mg/dL respectively. Phototherapy was used for unconjugated hyperbilirubinemia and CF was supposed to be the reason for conjugated hyperbilirubinemia, but in the second test total and conjugated bilirubin levels were increased to 25.94 and 18.38 mg/dL respectively. Checking the laboratory error resulted as the same findings. After this result, ultrasonography for hepatobiliary system was found to be normal. Thyroid hormone levels were evaluated and free thyronine (FT3) and free thyroxin (FT4) levels were 0.64 (n= 2.4-5.6 picog/mL) and 0.6 (n= 0.9-2.6 ng/dL) respectively. Thyroid stimulating hormone (TSH) and other thyroid test levels were normal at this evaluation. CH was diagnosed and levothyroxin treatment was begun with 10 microgram/dL. In the third day of the treatment total and conjugated bilirubin levels decreased to 11.16 and 10.97 mg/dL respectively. FT3, FT4 and TSH levels were 0.94 picog/mL, 0.4 ng/dL and 76.06 (n= 1.7-9.1 µU/mL) respectively. As TSH level was high, we increased the dose of levothyroxin to 15 µg/dL. Seven days later the last treatment dose FT3, FT4 and TSH levels were 3.98 picog/mL, 1.67 ng/dL and 6.97 µU/mL respectively. Pancreatic enzyme replacement regimen was also begun as soon as possible.

Jejunostomy was closed in the 3rd week of the patients' hospitalization.

DISCUSSION

As conjugated hyperbilirubinemia was occurred early in the postoperative time, anesthesia induced liver damage was strongly suggested and ultrasonographic examination was performed for acute liver damage which was ended normal. In fact, after the evaluation of the literature, we only found halothane induced bilirubinemia in children (8). We found no other reports that could explain hyperbilirubinemia in our anesthesia management. So, we evaluated other possibilities.

CF can also cause conjugated hyperbilirubinemia (9). CF is an autosomal recessive disorder in caucasian children with an incidence of 1 in 2500 (1). The CF gene is located on the long arm of chromosome 7 encoding the CF transmembrane conductance regulator (CFTR) protein, which is essential in the regulation of chloride transport in epithelial cells (1). Different haplotypic variants for CF chromosomes, suggesting that MI might constitute a specific clinical and genetic entity were studied (3). MI is congenital intestinal obstruction in which the meconium of the fetus occludes the bowel lumen in the distal ileum (4). It is often the earliest presentation of CF (1). Genetic differences associated with mutations of the CFTR gene may be the reason for predisposition to MI (2). One of the mechanisms of the conjugated hyperbilirubinemia is intestinal obstruction like MI caused by CF but to our knowledge, there also has not been a report for high levels of conjugated hyperbilirubinemia with CF as in our patient.

Presences of modifier genes which may also cause lung diseases are shown in MI patients (2). Some other anomalies of gastrointestinal system, lungs, and inguinal region were associated with CF in literature (4). Nevertheless, association of CF with a primary congenital hypothyroidism (CH) is not reported. Besides, in conjugated hyperbilirubinemia, hypothyroidism has to be rule out (9). Most cases of CH are due to thyroid dysgenesis, and only 2% are caused by genetic mutations and 10-15% of all cases are caused by genetic defects in the hypothalamic-pituitary-thyroid axis involving thyroid hormonogenesis and action (10). Also mutations in the genes encoding transcription factors or the TSH receptor cause thyroid dysgenesis in humans or in mouse models (6). Genetic factors in the pathogenesis of

congenital hypothyroidism were detected with some associated anomalies (11). In the last decade congenital defects like cardiac nervous system and eyes were detected with CH (6). Olivieri-Stazi et al, reported 7 of 1372 CH patients have congenital digestive system anomaly but details were not given in their study (6).

In short, congenital hypothyroidism may be evaluated for the patients with CF when conjugated hyperbilirubinemia is detected but we can not find a report defining association of MI and CH together. This is the first report for this coexistence and according to the known mechanisms of these two entities; we can say that there may not be a common mechanism for an association. Our patient may only be a sporadic case.

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