



CASE REPORT

THE ASSOCIATION OF COMMON ATRIUM WITH SMITH-LEMLI-OPITZ SYNDROME IN AN INFANT

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ABSTRACT

Smith-Lemli-Opitz syndrome is a rare syndrome presenting with multiple congenital anomalies/mental retardation associated with low plasma cholesterol levels. The spectrum of severity extends from prenatal death with holoprosencephaly or other lethal malformations, to patients with minimal physical abnormalities and normal intelligence or minimal intellectual impairment. Congenital heart defect is found in half of the Smith-Lemli-Opitz syndrome patients. To our knowledge, the association of common atrium and Smith-Lemli-Opitz syndrome has not been described before in the medical literature. We present a 4-month-old infant case of such association.

Keywords: Smith-Lemli-Opitz syndrome, Common atrium, Infant

BİR İNFANTTA SMITH-LEMLI-OPITZ SENDROMU VE ORTAK ATRİUM BİRLİKTELİĞİ

ÖZET

Smith-Lemli-Opitz sendromu düşük plazma kolesterol düzeylerinin eşlik ettiği çoklu doğumsal anomali/mental gerilik ile kendini gösteren nadir bir sendromdur. Klinik spektrum holoprozonsefali ya da letal malformasyonlarla prenatal ölümden normal zeka ya da hafif zihinsel bozukluk ve hafif fiziksel anormallliği olan hastalara kadar değişmektedir. Doğumsal kalp hastalığı Smith-Lemli-Opitz sendromlu hastaların yarısında bulunmaktadır. Bilgilerimize göre, Smith-Lemli-Opitz sendromu ve ortak atrium birlikteliği tıp literatüründe daha önceden açıklanmamıştır. Böyle birlikteliğin olduğu 4 aylık infant olguyu sunuyoruz.

Anahtar Kelimeler: Smith-Lemli-Opitz sendromu, Ortak atrium, İnfant

INTRODUCTION

Smith-Lemli-Opitz syndrome is an autosomal recessive, multiple congenital anomaly syndrome caused by deficiency of 7-dehydrocholesterol reductase, which catalyzes the last step of endogenous cholesterol synthesis.^{1,2} The estimated clinical incidence of this disorder is 1/25,000–1/60,000.^{3,4} Malformations observed in the Smith-Lemli-Opitz syndrome include Y-shaped 2-3 toe

syndactyly, polydactyly, unilobate lungs, renal dysplasia or agenesis, Hirschsprung disease, complex cardiac malformations, cataracts, central nervous system malformations; such as microcephaly and agenesis of corpus callosum; oropharyngeal malformations (cleft palate), genital ambiguity in genetic males, and facial abnormalities such as anteverted nostrils, micrognathia, and apparently low-set ears.³⁻⁵ There are no descriptions in the literature of

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common atrium associated with Smith-Lemli-Opitz syndrome. We present a case of such association.

CASE REPORT

A 4-month-old boy was admitted to the department of pediatric endocrinology because of inadequate weight gain. The pregnancy was uneventful. He was a term, live born infant. The infant weighted 2500 grams. He was the 3rd child of a consanguineous couple. At the age of 1, the first boy of the couple was deceased from an unknown illness. His physical examination revealed: weight: 2690grams (<3 p); height 50 cm (<3 p); head circumference: 33 cm (<3 p); pulse rate: 128/min; respiratory rate: 32/min; blood pressure: 80/65 mm/Hg and temperature: 37 C°. A cleft palate and abnormal oropharynx were noted. The infant had upward slanting palpebral fissures, a flattened nose, and a small tongue, mouth and mandible. The ears were angulated posteriorly. The infant had bilateral 2-3-4. toe syndactyly and clinodactyly of both second toes, perineal hypospadias, and bilateral cryptorchidism, small penis measured as 1 cm (normal is 2.5 cm according to age). The infant had bilateral 2-3-4. fingers overlapped (Fig. 1a, b). The rest of the physical examination was unremarkable. Laboratory examinations including complete blood count, serum electrolytes, liver function tests were all within normal limits. Total cholesterol, LDL-cholesterol and HDL-cholesterol were 38 mg/dl (<3 p), 30mg/dl (<3 p), 12 mg/dL (<3 p), respectively. In endocrinological evaluation, the values of hormones measured were FSH: 1.42 mIU/ml (normal, 0.16-4.1), LH: 6.542 mIU/ml (normal, 0.02-7.0), testosterone: 39 ng/dl, free testosterone: 1.7 pg/ml (normal, 0.7-14), DHEA-S: <15 µg/dl (normal, 5-11), cortisol: 13.4 µg/dl (normal, 2.8-23). The results of ACTH tests performed in order to rule out clinically-suspected congenital adrenocortical hyperplasia were normal. Moreover, hCG stimulation test was also normal. Karyotype was normal, 46, XY. Abdomen and renal ultrasounds were normal.



Figure 1a, b: Male patient showing facial and toe dysmorphic features suggestive for Smith-Lemli-Opitz syndrome.

Echocardiographic examination had demonstrated enlargement of the right ventricle and the right atrium, furthermore, the common atrium comprising both the right and left atrium (Fig. 2). The diagnosis of Smith-Lemli-Opitz syndrome accompanied by the common atrium was made on the basis of the patient's clinical features and laboratory findings. The patient was treated with dietary cholesterol supplementation (a boiled yolk per day) and has been followed-up by our pediatric endocrinology department.

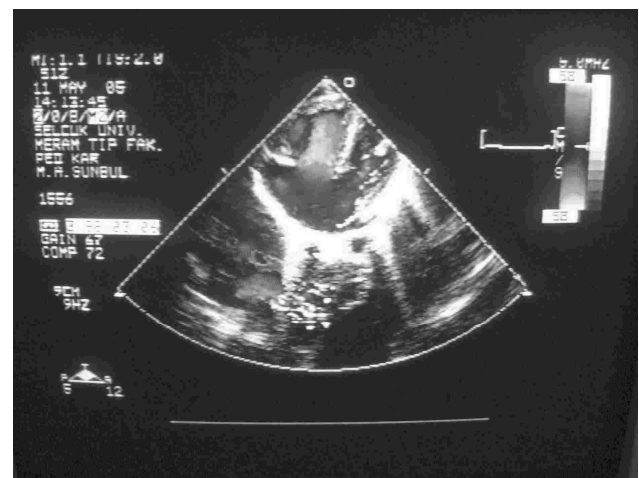


Figure 2: Echocardiography demonstrates common atrium



DISCUSSION

To our knowledge, the association of common atrium and Smith-Lemli-Opitz syndrome has not been described before in the medical literature. The phenotypic spectrum ranged from isolated syndactyly of toes 2 and 3 to holoprosencephaly and multiple visceral anomalies resulting in death in utero.⁵ Physical examination of the infant showed short stature, polydactyly with clinodactyly, overlapping of the fingers, perineal hypospadias, bilateral cryptorchidism, small penis and cleft palate which are characteristics of Smith-Lemli-Opitz syndrome.

Most patients with Smith-Lemli-Opitz syndrome have abnormally low plasma cholesterol levels and virtually all have elevated levels of the immediate precursor, 7-dehydrocholesterol (7DHC).⁶ Plasma cholesterol concentration is inversely correlated with clinical severity. Little relationship is seen between severity score and 7-dehydrocholesterol concentration.⁵ This infant had a low plasma cholesterol level (38 mg/dl), too.

Congenital heart defect is found in half of the Smith-Lemli-Opitz syndrome patients, and a specific association with atrioventricular canal defect and anomalous pulmonary venous return has been demonstrated. Common atrium is a rare variety of interatrial communication characterised by absence or virtual absence of the atrial septum, vestigial remnants of which may be occasionally present. Left axis deviation of the QRS complex is usually seen in the electrocardiography. A common atrium is much more commonly seen in the setting of an atrioventricular septal defect, particularly when there is coexisting atrial isomerism.⁷ In the infant, the diagnosis of common atrium was made on echocardiography.

Opitz et al. described a case which involved an enlarged third ventricle, thickening of the myocardium and autopsy documented a large secundum atrial septal defect, muscular ventricular septal defect, hypertrophy of the left ventricle and enlargement of the right ventricle.⁸ Of patients with Ellis-van Creveld syndrome, 50-60% have a heart defect; the most common anomaly is a common atrium

(40%).⁷ However, Ellis-van Creveld syndrome was excluded by clinical features and laboratory results in this patient.

Cholesterol supplementation has been used for several years to treat symptoms of Smith-Lemli-Opitz syndrome. Observational studies suggest that dietary cholesterol supplementation is beneficial; however, dietary cholesterol supplementation has some limitations such as not to cross the blood-brain barrier and not completely suppress the potential toxic effects of 7DHC.^{9,10} The use of HMG-CoA reductase inhibitors to reduce 7DHC levels in Smith-Lemli-Opitz syndrome has also been proposed and tested in two small trials with divergent outcomes.¹¹ This infant was treated with only dietary cholesterol supplementation.

In conclusion, careful dysmorphological examination should be performed in all patients presenting with dysmorphic features to diagnose as Smith-Lemli-Opitz syndrome. In addition, patients diagnosed as Smith-Lemli-Opitz syndrome; should be evaluated for congenital heart defect.

Smith-Lemli-Opitz syndrome is inherited in autosomal recessive form and consanguineous marriages are common in our country with a ratio of 20%. Therefore, this syndrome may be more common in Turkish population. In addition, the first child of this parents might have had the same syndrome. Families having a child with autosomal recessive disorder due to consanguineous marriages should be informed about genetic counselling. Because prenatal diagnosis is available, families having a child with this syndrome should be informed about genetic counselling.

REFERENCES

1. Smith DW, Lemli L, Opitz JM. A newly recognized syndrome of multiple congenital anomalies. *J Pediatr* 1964; 64:210-217.
2. Tint GS, Irons M, Elias ER, et al. Defective cholesterol biosynthesis associated with the Smith-Lemli-Opitz syndrome. *N Engl J Med* 1994; 330:107-113.
3. Kelley RI, Herman GE. Inborn errors of sterol biosynthesis. *Annu Rev Genom Hum Genet* 2001; 2:299-341.



4. Nowaczyk MJ, McCaughey D, Whelan DT, Porter FD. Incidence of Smith–Lemli–Opitz syndrome in Ontario, Canada. *Am J Med Genet* 2001; 102:18–20.
5. Cunniff C, Kratz LE, Moser A, Natowicz MR, Kelley RI. Clinical and biochemical spectrum of patients with RSH/Smith-Lemli-Opitz syndrome and abnormal cholesterol metabolism. *Am J Med Genet* 1997; 68:263–269.
6. Tint GS, Irons M, Elias ER, et al. Defective cholesterol biosynthesis associated with the Smith-Lemli-Opitz syndrome. *N Engl J Med* 1994; 330:107–113.
7. Sajeev CG, Roy TN, Venugopal K. Images in cardiology: Common atrium in a child with Ellis-Van Creveld syndrome. *Heart* 2002; 88:142.
8. .Opitz JM, Gilbert-Barness E, Ackerman J, Lowichik A. Cholesterol and development: The RSH (“Smith-Lemli-Opitz”) syndrome and related conditions. *Pediatr Pathol Mole Med* 2002; 21:153–181.
9. Irons M, Elias ER, Abuelo D, et al Treatment of Smith–Lemli–Opitz syndrome: results of a multicenter trial. *Am J Med Genet* 1997; 68:311–314.
10. Nwokoro NA, Mulvihill JJ. Cholesterol and bile acid replacement therapy in children and adults with Smith–Lemli–Opitz (SLO/RSH) syndrome. *Am J Med Genet* 1997; 68:315–321.
11. Jira P, Wevers R, de Jong J, Rubio-Gozalbo E, Smeitink J. New treatment strategy for Smith–Lemli–Opitz syndrome. *Lancet* 1997; 349:1222.