CLINICAL STUDY

Trisomy 18 mimicking Smith–Lemli–Opitz syndrome in the immediate neonatal period

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Abstract

The study describes a dysmorphic newborn infant with life-threating anomaly, later diagnosed as trisomy 18, mimicking Smith–Lemli–Opitz syndrome in the immediate neonatal period. The establishment of the correct diagnosis in the first days of life is very important for the decision-making process, because trisomy 18 has a poor prognosis, and treatment is not instituted, whereas cholesterol supplementation may be of benefit to patients with Smith–Lemli–Opitz syndrome. Ultraviolet spectrophotometry showed very easy and rapid method for differentiation of both syndromes, where gas chromatography/mass spectrometry analysis is not available. ***(Fig. 2, Ref. 18.)***
Key words: trisomy 18, Smith–Lemli–Opitz syndrome, ultraviolet spectrophotometry, dysmorphic newborn infant.

Newborns with multiple congenital anomalies often require prompt medical or surgical intervention for immediate neonatal problems such as congenital heart disease, respiratory distress syndrome, or gastrointestinal obstruction. In our case report we present a dysmorphic newborn infant with trisomy 18 and a surgically correctable anomaly, mimicking Smith–Lemli–Opitz syndrome (SLOS) in immediate neonatal period.

Case report

The patient, a boy, was the first child of non-consanguineous parents, born after an uneventful pregnancy and delivery. He weighed 2280 g at birth and had many dysmorphic features (microcephaly with hypoplasia of orbital ridges, hypertelorism, anteverted nares,low set ears, micrognathia (Fig. 1), syndactyly of second and third toes, short dorsiflexed big toes (Fig. 2), female external genitalia with hypoplasia of labia majora). Shortly after the birth, the newborn presented dramatical cyanosis and severe respiratory distress, requiring arteficial ventilation. On the basis of chest radiography, diaphragmatic hernia was suspected. Echocardiogram disclosed tetralogy of Fallot. Bronchography revealed right-sided diaphragmatic hernia with hypoplasia and atelectasis of the lung on the opposite side. Laboratory biochemical examination showed a plasma cholesterol 1.21 mmol/l, measured by enzymatic assay. These clinical and biochemical findings suggested the diagnosis of Smith–Lemli–Opitz syndrome (SLOS). Ultraviolet spectrophotometry (UVS) as a biochemical screening procedure of SLOS was indicated. After the prompt and aggressive preoperative care the clinical state of the child stabilized, so the surgical reconstruction could be postponed, until chromosome results became available. The routine karyotype analysis revealed supernumerary eighteenth chromosome with XX constitution. After the diagnosis of trisomy 18 was made, a surgical treatment was not instituted. Patient died at the age of 18 days. An autopsy confirmed right-sided diaphragmatic hernia and tetralogy of Fallot. The liver, which partially blocked the pleuroperitoneal canal, limited the amount of bowel that can herniate into chest. It explained the less severe symptoms, resulting in postponement of the operation.

Discussion

A suspicion of SLOS in the first days of life of our high-risk newborn infant was made on the basis of some dysmorphic facial features, syndactyly of 2–3 toes and mild anomaly of exter-

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nal genitalia. The relatively low plasma cholesterol measured by enzymatic method supported this diagnosis.

Until 1994 there was no laboratory or biochemical test available to diagnose SLOS. The discovered defect of cholesterol biosynthesis (1) provided a useful biochemical tool for the statement of precise diagnosis. The typical biochemical profile of SLOS patients shows low serum cholesterol, and abnormally high 7-dehydrocholesterol (7-DHC) and 8-dehydrocholesterol levels measured by gas chromatography/mass spectrometry (GC-MS) (2). Since 7-DHC show a typical ultraviolet absorption spectrum (3, 4), we use this method as a biochemical screening procedure for this syndrome. It has been suggested that the ultraviolet spectrophotometry, an easy test for accumulation of 7-DHC, should be always coupled with the measurement of plasma cholesterol level, should SLOS be suspected (5).

Despite the relative low plasma cholesterol in our newborn, we did not confirm the accumulation of 7-DHC, the immediate precursor of cholesterol in its biosynthetic pathway. Until now, there have been very few data available for the reference range of plasma cholesterol in healthy newborns, and as the pediatricians were not aware of reference ranges of cholesterol in healthy newborns, (6) they developed reference ranges for cholesterol within cord blood and neonatal sera from 150 healthy infants collected in the first week of life. The cholesterol levels at birth were low (mean: 1.6 mmol/l) with a wide range (0.5–3.2 mmol/l),

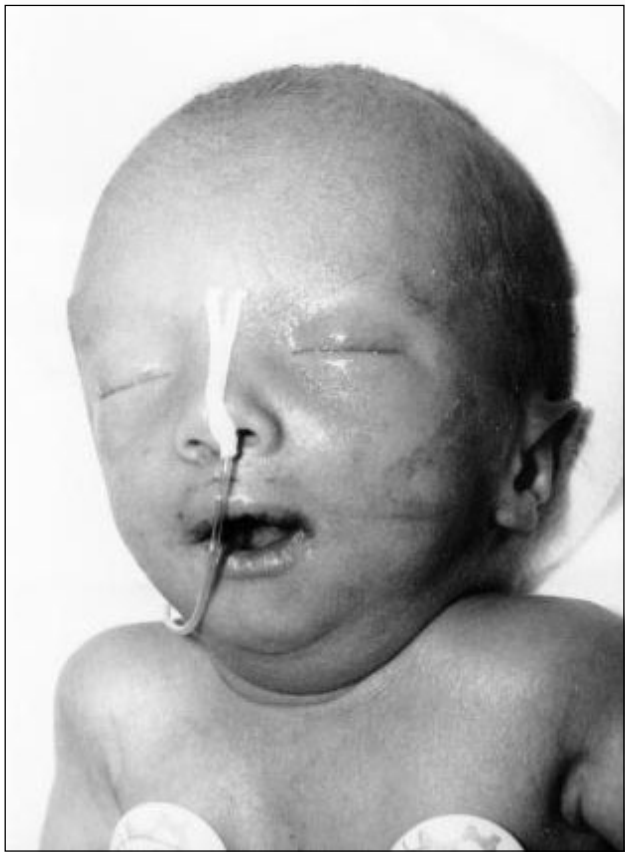

Fig. 1. Facial dysmorphic features of the newborn.

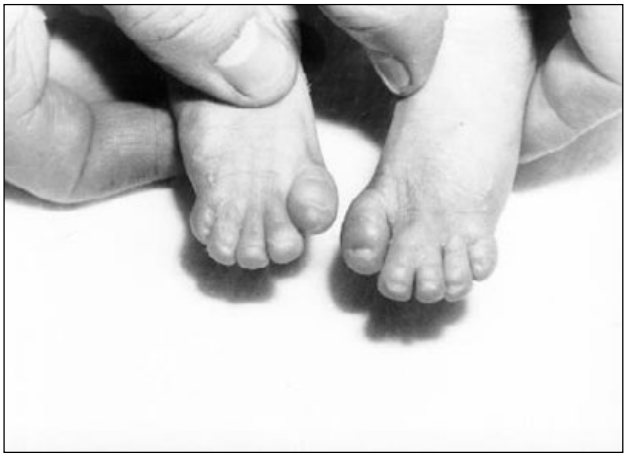

Fig. 2. Syndactyly of 2–3 toes and short dorsiflexed big toes.

and increased rapidly during the first week of life to almost doubled values (mean: 2.9, range: 1.7–4.2 mmol/l). So our plasma cholesterol measured by the enzymatic method, was within the reference range.

Trisomy 18 is a lethal anomaly with more than 130 different abnormalities (7). The newborns with trisomy 18 suffer also from growth retardation, characteristic facial appearence with microcephaly and small chin, low set ears, narrow palatal arch or rare cleft palate, cardiac defects, genital malformations (cryptorchism, hypospadia) and anomalies of hands and feet (ulnar or radial deviation of hand, simian crease, also syndactyly of second and third toes) (7, 8). Many abnormalities of patients with trisomy 18 require surgical correction during the neonatal period. The confirmation of the diagnosis of trisomy 18 depends on the demonstration of supernumerary eighteenth chromosome (9), and the routine karyotype analysis requires minimum processing time of 4 days. The decision-making process is very important, because in the case of trisomy 18, surgery may then be witheld (10). A newborn infant with trisomy 18 should be considered as a patient with a hopeless outlook, who ought not to be subjected to invasive procedures. In newborns with SLOS, the pediatric surgeon may be the first to be consulted (11). However in spite of trisomy 18, the prognosis of SLOS depends on the extent of internal malformations and on the degree of enzyme deficiency. Early administration of cholesterol is indicated in every case.

Both syndromes have a wide clinical spectrum, share no single pathognomonic feature (12, 9), and have relatively high incidence. Trisomy 18 is the second most common syndrome of autosomal trisomy syndromes, with an estimated incidence between 1 in 4000 and 1 in 8000 births (13). The incidence of SLOS is estimated to range from 1/20 000 to 1/40 000 among the newborns of European origin (14, 15). For almost 30 years following its description in 1964, SLOS was just one of many autosomal recessive, multiple anomaly syndromes and as such caused a little interest. But after an important biochemical discovery in 1993 (1) SLOS was abruptly lifted from its relative obscurity (16) and it is now the best example of a syndrome, in which

a discrete block in a single metabolic pathway leads to severe malformations (17, 18).

Many malformation syndromes, for instance trisomy 18, share at least some of the clinical features of SLOS. The UVS determination of serum sterols is a reliable, cheap and quick test in the determination or exclusion of SLOS when the GC-MS analysis is not available.

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