A 34-week-old male fetus with short rib polydactyly syndrome (SRPS) type I (Saldino-Noonan) with pancreatic cysts

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SUMMARY: Balcı S, Altınok G, Tekşen F, Eryılmaz M. A 34-week-old male fetus with short rib polydactyly syndrome (SRPS) type I (Saldino-Noonan) with pancreatic cysts. Turk J Pediatr 2003; 45: 174-178.

A 34-week-old male fetus (first diagnosed at 28 weeks of gestation) with short rib polydactyly type I Saldino-Noonan syndrome is presented in this study. In the postmortem examination of the fetus, pancreatic dysplasia, multiple cysts and multicystic dysplastic kidneys, omphalomesenteric cyst, ascites, malrotation, micropenis, undescended testes, bilateral inguinal hernia and hydrops were observed. The parents were first-degree cousins. One male and one female sibling had similar findings and both had died after birth. Only a four-year-old healthy daughter was alive.

We believe these findings will be helpful in the differential diagnosis of further lethal skeletal dysplasia cases.

Key words: Saldino-Noonan syndrome (SRPS type I), pancreatic cysts, autosomal recessive inheritance.

Short rib polydactyly syndrome (SRPS) type I, described by Saldino-Noonan[1], is characterized by severe thoracic dystrophy with striking micromelia, postaxial polydactyly, metaphyseal irregularities of long bones, visceral abnormalities, cardiac defects, malrotation, and imperforate anus. The mode of inheritance of SRPS type I is autosomal recessive.

Short rib polydactyly syndromes are of at least seven types but the identification of the type has sometimes been difficult as some cases show marked clinical and pathological overlaps[2]. The problem of whether SRPS is a single gene or a heterogeneous entity may be solved by further molecular studies[3].

In this report, we present the prenatal diagnosis of a 34-week-old male fetus with SRPS type I, associated with pancreatic cysts measuring 0.3 x 0.1 cm in diameter. Although this association has been reported previously in the Saldino-Noonan syndrome (SRPS type I)[4], it is not very common. For this reason, the prenatal diagnosis of pancreatic cysts in cases with lethal skeletal dysplasia seems to be very important in the early differential diagnosis of SRPS type I.

Case Report

Our case was a male stillbirth at 34 weeks of gestation who was the fourth-born child of consanguineous parents. The mother was 25 and the father 34 years old. The prenatal history of this fourth child revealed the presence of severe thoracal hypoplasia, oligohydramnios, ascites, and increased renal echogenicity during the ultrasonographic examination at 28 weeks of gestation.

No attempt was made after these findings to terminate the pregnancy due to the parents' refusal.

The family history revealed that the first female and the third male siblings were also stillborn and had similar clinical findings but no specific diagnosis had been made in these affected siblings again because of the refusal for autopsy.

The male fetus was stillborn at 34 weeks of gestation. His weight was 2,490 g and length 35.5 cm, which was below the 3rd percentile. Circumference of the head, chest and the abdomen were 31, 28 and 34 cm, respectively.

The phenotypic appearance of the fetus was characterized by the narrow thorax, short neck, short limbs, protuberant abdomen, bilateral postaxial polydactyly and bilateral Simian lines on both hands, hypoplastic penis , undescended testes and bilateral inguinal hernia (Fig. 1a). A plethoric facial appearance, short neck and low-set ears were also noted (Fig. 1b). Bilateral postaxial polydactyly was present on both feet (Fig. 2). Marked edema was observed over the scalp, face and neck. He also had severe micromelic dwarfism with a flattened face and markedly low-set hypoplastic ears.

The postmortem body X-ray showed very short, horizontal ribs, metaphyseal irregularities of long bones and severe bowing of the radii and ulnae (Fig. 3). Postmortem cranial tomography showed pachygyria (Fig. 4a) and a septum pellucidum cyst (Fig. 4b).

Autopsy revealed that the lungs were hypoplastic but there was no cardiovascular abnormality. The abdominal cavity contained 20 ml ascites and an omphalomesenteric cyst was present behind

Fig. 1a. Postmortem photograph of the fetus. Note the narrow thorax, short limbs, postaxial polydactyly, bilateral Simian line, hypoplastic penis and bilateral inguinal hernia.

Fig. 1b. Plethoric facial appearance, short neck and low-set ears.

Fig. 2. Postaxial polydactyly of feet.

Fig. 3. Radiographs of fetus showing short, horizontal ribs, metaphyseal irregularities of long bones, triangular ossification defects of acetabulum, and bowing of the radii and ulnae.

Fig. 4a. Postmortem computerized tomography (CT) showed pachygyria.

Fig. 4b. Septum pellucidum cyst.

the intestinal loops. Malrotation was detected, with the appendix vermiformis in the left lower quadrant. Bilateral multicystic dysplastic kidneys displayed numerous cysts ranging in size from 0.2 to 0.3 cm (Fig. 5). Bilateral ureters and bladder were found to be normal. The cut surface of the enlarged pancreas showed multiple cysts with the largest cyst measuring 0.3 cm (Fig. 6). Microscopically, both kidneys revealed immature mesenchymal stroma with areas of cartilage and cystically dilated tubules surrounded by scattered intact glomeruli (Fig. 7). Cystically dilated pancreatic ducts were surrounded by immature mesenchyma containing scattered pancreatic acini (Fig. 8). The structure of the liver and biliary system were unremarkable.

The postmortem chromosomal analysis of peripheral blood sample was found to be

Fig. 5. Bilateral renal multicystic dysplasia showing cysts 0.2 x 0.3 cm in size.

Fig. 6. Multicystic dysplasia of the pancreas showing cysts 0.1 x 0.3 cm in size.

Fig. 7. Bilateral renal cystic dysplasia characterized by the islands of cartilage, dilated tubules and immature mesenchyma (H+E, x115).

Fig. 8. Cystically dilated pancreatic ducts are surrounded by immature mesenchyma containing scattered pancreatic acini (H+E, x115).

normal (46, XY).

Discussion

Saldino-Noonan syndrome, originally described by Saldino-Noonan in 1972[1], is a very rare autosomal recessive lethal skeletal dysplasia characterized by hydrops and short stature. In the differential diagnosis of the SRPSs such as SRPS type II (Majewski), SRPS type III (Verma-Naumoff) and SRPS type IV (Beemer-Langer), the clinical, radiological and morphological findings are used. Saldino-Noonan syndrome is commonly associated with cardiac defects, including transposition of the great vessels, polycystic kidneys, hypoplastic penis or ambiguous genitalia. Gastrointestinal malformations are frequently observed, such as intestinal malrotations or imperforate anus, as in our case. Previously, malrotation was published both in Saldino-Noonan syndrome[5] and in Beemer-Langer type with polydactyly[6], while short intestine and pyloric stenosis were also reported in Beemer-Langer type syndrome[7].

The association of short rib syndrome with dysplastic and cystic kidney[8-11], has been more commonly reported in cases of skeletal dysplasia, but pancreatic dysplasia and cysts have been very rarely observed[8]. Cicediyan et al.[12] reported a new short rib syndrome (type IV Beemer-Langer) with ambiguous genitalia, anophthalmia, cleft lip/palate, congenital hepatic fibrosis, pancreatic cystic dysplasia, pulmonary hypoplasia and renal dysplasia. Cystic dysplastic pancreas was also observed in type II Majewski syndrome[13] and

in asphyxiating thoracic dysplasia (Jeune) syndrome. In another study, Fraser et al.[14] reported a case with chondrodysplasia, situs inversus totalis, cleft epiglottis and larynx, hexadactyly of hands and feet, pancreatic cystic dysplasia, renal dysplasia/absence, micropenis, ambiguous genitalia and imperforate anus. For this reason, in every lethal skeletal dysplasia case, an autopsy should be performed to determine whether or not any internal malformation is present.

The most interesting finding of this new case with Saldino-Noonan syndrome was its association with pancreatic cysts because to our knowledge this finding has only very rarely been observed.

Interestingly, the family history of our patient showed two stillborn siblings (one male and one female). These siblings had similar clinical findings, such as short limb lethal dysplasia, but unfortunately no postmortem X-ray or physical examination was available. The presence of consanguinity between the parents and the positive history of affected siblings also suggested the autosomal recessive mode of inheritance. It has been shown that prenatal detection of pancreatic cysts and short limb dwarfism is possible[15]. A Saldino-Noonan syndrome was diagnosed prenatally at 17 weeks of gestation[16] and recently another case was diagnosed by transvaginal sonography as early as 13 weeks of gestation[17].

Finally, it was concluded that demonstration of pancreatic dysplasia and cysts in Saldino-Noonan syndrome was very important in the early prenatal detection. Pancreatic dysplasia and cysts have only rarely been observed in a few cases of skeletal dysplasias, but we believe that this association will be much more commonly displayed with the recent advent in technologies in ultrasonography and with meticulously performed postmortem examination.

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