

Case report

Prenatal diagnosis of Neu-Laxova syndrome: a case report

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Abstract

Background: Neu-Laxova syndrome is a rare congenital abnormality involving multiple systems. We report a case of Neu-Laxova syndrome (NLS) diagnosed prenatally by ultrasound examination.

Case presentation: A 29-year-old gravida 3, para 2 woman was first seen in our antenatal clinic at 38 weeks' pregnancy. Except for the consanguinity and two previous abnormal stillborn babies her medical history was unremarkable. On ultrasound examination microcephaly, flat forehead, micrognathia, intrauterine growth restriction, generalized edema of the skin, hypoplastic chest, excessive soft tissue deposition of hands and feet, joint contractures and a penis without scrotal sacs were detected. She delivered a 2000 g male fetus. He died five minutes after delivery. Postmortem examination confirmed the diagnosis of Neu-Laxova syndrome.

Conclusion: Because of the autosomal recessive inheritance of Neu-Laxova syndrome genetic counseling and early-serial ultrasound examination should be performed at risk families. Early diagnosis of the disease may offer termination of the pregnancy as an option.

Background

Neu-Laxova syndrome is a lethal disorder with multiple abnormalities. It was first reported by Neu et al. [1], in 1971. Approximately 40 cases have been reported to date [2,3]. We present a case of Neu-Laxova syndrome which was diagnosed *in utero* by ultrasound examination.

Case presentation

A 29-year-old gravida 3, para 2 Turkish woman was first seen at our antenatal clinic at 38 weeks' of gestation. Her past medical history was remarkable for consanguinity (cousin) and two spontaneous delivery of abnormal infants.

Ultrasound examination revealed a single fetus and marked polyhydramnios. Fetal biometry showed a biparietal diameter of 53 mm (21 weeks \pm 2 days) and femur length of 55 mm (28 weeks \pm 2 days). Microcephaly, flat forehead, micrognathia, generalized edema of the skin, hypoplastic chest (Figure 1), excessive soft tissue deposition of hands and feet (Figure 2), and joint contractures (Figure 3) were detected. A curved penis without scrotal sacs was observed.

After induction of labor she delivered a male infant weighing 2000 g. He died five minutes after delivery. The neonatal examination confirmed all the sonographically



Figure 1
Sagittal section of the fetal trunk. Note the hypoplastic thorax (thin arrows) and abdomen (thick arrows).

detected malformations. On postmortem examination of the neonate microcephaly, sloping forehead, ocular hypertelorism, protruding eyes with absent lids, micrognathia, short neck, ichthyosis, scaling edematous skin, excessive edema of hands and feet, flexion contractures, undescended testes were detected (Figure 4). An x-ray film of the infant revealed microcephaly (Figure 5), and a S-shaped spine.

Neu-Laxova syndrome is a rare congenital abnormality characterised by intrauterine growth restriction, microcephaly, facial dysmorphism, short neck, edema, scaly skin and perinatal death [4]. Additional features such as spina bifida, cryptorchidism and shallow orbital cavities have been reported. Chromosomal analysis in reported cases

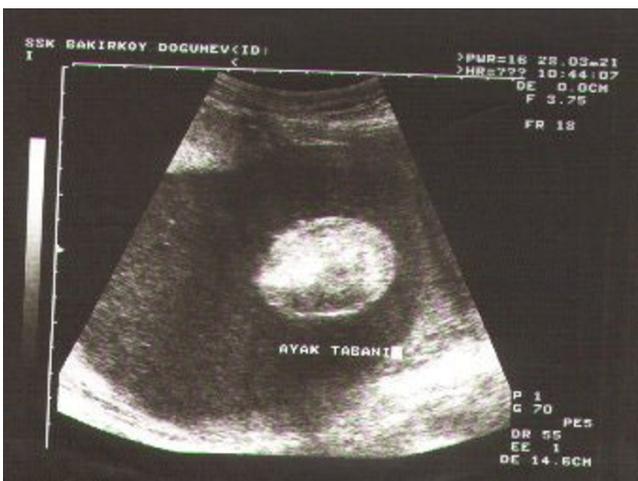


Figure 2
Excessive soft tissue deposition in the foot.



Figure 3
Flexion contractures of the lower limb (arrow: knee).

has revealed a normal karyotype and an autosomal recessive inheritance has been postulated [5].

The pathologic abnormalities observed in Neu-Laxova syndrome appear to be a result of neuro-ectodermal dysplasia as evidenced by lack of brain development, eye abnormality, absence of hair and hyperkeratosis [6].

In this case the affected fetus which was born after two stillborn infants with similar abnormalities supports the autosomal recessive mode of inheritance. Neu-Laxova syndrome has been diagnosed in the offspring of both consanguineous and nonconsanguineous couples.

Prenatal diagnosis of the syndrome has been reported with an emphasis on ultrasonographic findings. Gulmezoglu *et al.*, [7] showed that the specific features of the syndrome make possible the prenatal diagnosis based on the ultrasound findings.

At 32 weeks' of pregnancy Shapiro *et al.*, reported a case of prenatal ultrasonographic diagnosis of Neu-Laxova syndrome with Dandy-Walker malformation and choroid plexus cysts as new findings. It was interesting to note that there was marked edema in the scalp but not in hands and feet. The case was presented as an example for the question of phenotypic variability in Neu-Laxova syndrome [8]. Pulmonary hypoplasia, and hyperechoic calvaria, associated with acoustic shadowing which obscures any intracranial abnormality was reported in Neu-Laxova syndrome [9,10]. Other CNS abnormalities include lissencephaly, microgyria, hypoplastic cerebellum, abnormalities of corpus callosum and lateral ventricles and aplasia of olfactory structures and the optic nerves. It is important to be aware that, on coronal sonographic sec-



Figure 4
Photograph of the neonate with the Neu-Laxova syndrome. Note the micrognathia, absent eyelids, scaly skin, ichthyosis and edema of the hands and feet.

tions NLS may resemble anencephaly because of sharply receding forehead [11].

Serial ultrasonographic examination beginning at approximately 28 weeks of gestation showed various ultrasonographic features of Neu-Laxova syndrome at different stages of pregnancy. From this point of view, it was suggested to monitor by ultrasonography at 6–8 weeks for accurate dating, at 12–16 weeks for active fetal limb movements and at 16–24 weeks for facial and skeletal anomalies, the detection of IUGR and polyhydramnios in risk group [9].

Rode *et al.*, have reported the mid-trimester prenatal diagnosis of Neu-Laxova syndrome in at risk families by serial ultrasonographic examinations. Growth curves derived from serial sonograms revealed abnormalities of all biometric measurements, most notable in BPD which were less than two standard deviations below the mean for all gestational ages. Although first-trimester ultrasonographic diagnosis of affected fetuses does not appear to be reliable, early pregnancy dating is critical to discriminate between early onset IUGR and incorrect dating. Second-trimester biometric measurements proved far more reliable. In addition to early severe IUGR, additional sonographic features were present in all affected fetuses. Increased nuchal thickness, abnormal position of hands and feet, and intracranial abnormalities were generally detected early in the second trimester [12].

These reports show the existing possibility of early diagnosis of Neu-Laxova syndrome by detecting the aberrant growth and anomalies.

Ultrasonographic features which have been described in NLS including the absence of breathing movements, sucking, swallowing, or normal isolated arm and leg movements may also be detected in the third trimester. These



Figure 5
X-ray film of the newborn.

findings are also suggestive of other fetal akinesia/hypokinesia disorders [13].

The differential diagnosis of the NLS should include cerebro-ocular-facial-skeletal (COFS) syndrome, Walker-Warburg syndrome, Pena-Shokeir phenotype, cerebro-arthrodigital syndrome, Smith-Lemli-Opitz syndrome and Miller-Dieker syndrome [14]. The prenatal diagnosis of Pena Shokeir phenotype has been reported at 14 weeks' of pregnancy, mainly based on an abnormal fetal movement profile, in association with abnormal position of the fetal limbs [15].

Walker-Warburg syndrome characterised by severe congenital oculo-cerebral abnormalities, including lissencephaly and ventriculomegaly has been diagnosed as early as in the first trimester especially in cases involving severe intracranial anomalies, such as encephalocele. Microcephaly and IUGR are the features of both Smith-Lemli-Opitz and Miller-Dieker syndrome. All these phenotypes have common abnormalities but the presence of excessive subcutaneous tissue deposition with edema is a hallmark feature of Neu-Laxova syndrome. Intrauterine infections such as toxoplasmosis, rubella and varicella can also feature microcephaly and should be considered [16].

Conclusion

Early diagnosis of this condition is important because it can offer termination of pregnancy for a lethal disease. Genetic counseling and early-serial ultrasound examination should be performed at risk families because of the autosomal recessive mode of inheritance.

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Written consent was obtained from the patient or their relative for publication of the patient's details.

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