Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2020, 10, 341-347
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

A Case of Complete Neu-Laxova Syndrome: Report and Literature Review

Bouchra Fakhir[1], Oussama Rachid[1*], Amal Ait Benhassi[1], Nisrine Aboussair[2], Abderraouf Soummani[1]

[1]Department of Gynecology & Obstetrics, University Hospital Mohammed VI, Cadi Ayyad University, Marrakech, Morocco
[2]Department of Genetics, Clinical Research Center, University Hospital Mohammed VI, Cadi Ayyad University, Marrakech, Morocco

Email: *oussama.rachid@edu.uca.ac.ma

How to cite this paper: Fakhir, B., Rachid, O., Benhassi, A.A., Aboussair, N. and Soummani, A. (2020) A Case of Complete Neu-Laxova Syndrome: Report and Literature Review. *Open Journal of Obstetrics and Gynecology*, **10**, 341-347.
https://doi.org/10.4236/ojog.2020.1030031

Received: February 8, 2020
Accepted: March 6, 2020
Published: March 9, 2020

Abstract

Neu-Laxova syndrome (NLS) is a rare autosomal recessive and early fatal disease. It is a complex entity that includes intrauterine growth retardation, abnormal facial structure, limb and skeletal abnormalities, and ichthyosis and severe malformations of the central nervous system. We report a rare case of recurrence of Neu-Laxova syndrome in a 32-year-old pauciparous woman, which occurred after a first cousin's consanguineous marriage. Typical ultrasound findings included hydramnios, severe intrauterine growth restriction, craniofacial and central nervous system abnormalities such as ventriculomegaly. The newborn shows a terrible face with a usual craniofacial aspect, eyeball proptosis, puffy hands and feet, large bilateral cleft lip/palate, severe hall body ichthyosis. The overcome was fatal, the death occurred in less than one hour after birth. Consanguinity remains the most implicated cause which is high in developing countries. Prenatal serial ultrasound examinations with genetic counselling should be performed on high-risk pregnant women to terminate affected pregnancies.

Keywords

Neu-Laxova Syndrome, Ichthyosis, Growth Retardation, Microcephaly, Polymalfomations

1. Introduction

Neu-Laxova syndrome (NLS) is a rare autosomal recessive lethal malformation complex.

It is clinically characterized by the appearance of scaly skin caused by a lack of

keratinization by an alteration of the differentiation of the epidermis associated with various malformation anomalies (facial and skeletal abnormalities and central nervous system affection).

Most cases have been described in couples with inbreeding, studies still underway to establish the causal link and which will allow possible genetic counselling.

We are describing a case of complete Neu laxova Syndrome.

2. Case Report

A 32-year-old woman with 2 living children 4 para 4 gravida, married to a 37-year-old man. The couple is healthy, related to first-degree cousin's relationship. The previous pregnancy gives a birth to a poly malformed new born with no further medical information and no other medical history was revealed. The pregnancy was unfollowed; She was addressed to our department for suspicion of foetal malformations, foetal growth restriction and hydramnios in a proposed at term and in labour pregnancy.

The ultrasound examination findings in prepartum included hydramnios, severe intra-uterine growth restriction, craniofacial and central nervous system anomalies. Foetal akinesia and foetal electrocardiogram showed no particularities.

The vaginal delivery took place without any incidents giving birth to an abnormal-like new born, female, Apgar 03/10 with birth weight at 1400 g.

On clinical examination, the new born present firstly a severe form of collodion type ichthyosis, it was the first sign that challenged us, we noticed a collodion-like greyish membrane on the head (Figure 1) and an ichthyotic, thick, stretched, tight skin lesions especially on the body.

He had also a very low birth weight; amnios fluid was abundant, not fetid Globally, the newborn present Microcephaly, extremely short neck, malformed

Figure 1. Anterior global view of the newborn showing global ichthyosis, oedema and puffy hand and feet.

low-set ears, kyphosis, general oedema, and short but normal umbilical cord (Figure 2).

Abnormal facial features include hypertelorism, slopping forehead, large malformed ears, manifest large bilateral cleft/lip palate, mouth open round, thick lips, whitish oedematous gums and micrognathia.

Newborn death occurs in less than one hour, probably due to chest immobility.

The examination of the eyes (Figure 3) was the most difficult. It was hard to find equivalent description in the literature. Absence of eyelids and iris, white opaque eyeball proptosis, due probably to massive oedema of eye's sclera and conjunctiva.

The newborn shows short upper limbs, that joining the trunk a distance from an erased shoulder.

The four limbs were in rigid flexion, oedematous shiny cardboard skin, presenting at their extremities a puffy hands and feet, erasing the normal shape of fingers and responsible for cutaneous syndactyly.

3. Discussion

NLS is a rare metabolic disease firstly reported by Neu *et al*. [1] 1971 and Laxova [2] 1972, that the implication of L-serine biosynthesis pathway has been proved in the last few years [3] [4].

This syndrome offers a wide range of Clinical features grouping numerous central nervous system anomalies: microcephaly, hypoplastic cerebellum, corpus

Figure 2. Profile view of the newborn showing kyphosis, short neck.

Figure 3. Eyes and face abnormalities.

callosum agenesis, decreased gyri, ventriculomegaly, Intrauterine growth retardation, skin findings: ichthyosis, oedema, collodion baby, dysmorphic manifestations: erased forehead, hypertelorism, ectropion, flat/abnormal nose, low/malformed ears, micrognathia, cleft lip/palate), Ocular features contain exophthalmos, absence of eyelids, and cataract, limb anomalies: flexion contractures, deformity of digits, deformity of limbs, syndactyly of fingers and toes, rocker bottom feet, and genital ambiguity [5] [6] [7] [8].

Fitch *et al.* [9] divided all the malformation anomalies into two specific and non-specific groups.

The first group of specific abnormalities includes spinal kyphosis, swelling of the limbs, oedema, and ichthyosis which remains the primary symptom.

These anomalies facilitate the identification of the syndrome and its clinical confirmation.

The second group of non-specific abnormalities includes short stature, hypertelorism, low ears, and micrognathia. According to the author, these anomalies are due to growth retardation.

Additionally, the ichthyotic skin changes are emphasized to be the characteristic manifestation; further the limb anomalies are attributed to reduced intrauterine movements due to tight skin, developing as a result of ichthyosis.

In our case, most of the characteristic findings of Neu-Laxova were observed such as central nervous system implication, hall body skin restriction with ichthyosis, intra-uterine growth restriction, facial, ocular and limb abnormalities.

However, lamellar ichthyosis was firstly the condition that we considered in the differential diagnosis. Our patient exhibited phenotypic characteristics, including collodion membrane in the head area, shiny stretched thick skin on the body, which was similar to lamellar ichthyosis.

History of consanguinity suggests an autosomal recessive inheritance in Neu-Laxova. In fact, this syndrome is frequently reported from countries with high rates of consanguineous marriages [10], such as Morocco. Indeed, parental

consanguinity was present in the majority of the cases reported. Karyotyping of affected cases has been reported to be normal on majority cases [6] [7] [8] [11].

Additionally, the literature [5] [6] shows mostly a history of previous spontaneous abortions. And/or similar cases, or new born death, which is our case.

In antenatal, ultrasound remains the most reliable for a diagnosis of NLS and also for adequate management, eventually pregnancy termination.

Differential diagnosis is set mainly with the other syndromes associations with a foetal hypo-akinesia such as cerebro-oculo-facio-skeletal syndrome, multiple pterygium syndrome, pena-shokeir syndrome type I, syndrome miller-dieker syndrome, that shares with the NLS particular anomalies such as IUGR, microcephaly, arthrogryposis and subcutaneous oedema [5] [7].

However, despite this phenotypic overlap, the finding of CNS anomalies and characteristic facial dysmorphia should lead us to think about the NLS on antenatal ultrasound [7] [12]. These anomalies should be easy to spot in the second trimester.

In family with high risk of NLS (similar case, consanguinity), these ultrasound signs are the more suggestive, thus, genetic counselling and proposition for pregnancy termination should be discussed with the couple.

Although, Muller proposed in his paper a protocol for ultrasound surveillance for NLS.

In our practice, such as the majority of cases in a developing country, this pregnancy was not followed. Obstetric sonography of first and second trimester was not realized, interfering with management and organization of the case study.

Genetic study is in progress to avoid other recidivisms for this couple. However histological and post mortem study of the new born was not performed.

Most infants with Neu-Laxova are stillborn or die soon after birth, within minutes to a few hours due to chest constriction, infection or neurologic complications [13] [14].

However, one of the original patients reported by Neu *et al.* [1] survived 7 weeks.

In our patient, the overcome was lethal in less than one hour.

4. Conclusions

Neu-Laxova syndrome is a rare and fatal disease, remains unknown by a large number of practitioners.

The positive diagnosis remains clinical postnatal. NLS should be included in the differential diagnosis of ichthyotic newborn.

Consent and Acknowledgements

The couple is consent for case report publication after we explained the importance of genetic counselling for following pregnancies. Photographies was taken after permission for scientific purposes only.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Neu, I.U., Kajii, T., Gardner, L.I., Nagyfy, S.F. and King, S. (1971) A Lethal Syndrome of Microcephaly with Multiple Congenital Anomalies in Three Siblings. *Pediatrics*, **47**, 610-612.

[2] Laxova, R., Ohara, P.T. and Timothy, J.A.D. (1972) A Further Example of a Lethal Autosomal Recessive Condition in Sibs. *Journal of Intellectual Disability Research*, **16**, 139-143. https://doi.org/10.1111/j.1365-2788.1972.tb01585.x

[3] Shaheen, R., Rahbeeni, Z., Alhashem, A., Faqeih, E., Zhao, Q., Xiong, Y., *et al*. (2014) Neu-Laxova Syndrome, an Inborn Error of Serine Metabolism, Is Caused by Mutations in *PHGDH*. *The American Journal of Human Genetics*, **94**, 898-904. https://doi.org/10.1016/j.ajhg.2014.04.015

[4] Acuna-Hidalgo, R., Schanze, D., Kariminejad, A., Nordgren, A., Kariminejad, M.H., Conner, P., *et al*. (2014) Neu-Laxova Syndrome Is a Heterogeneous Metabolic Disorder Caused by Defects in Enzymes of the L-Serine Biosynthesis Pathway. *The American Journal of Human Genetics*, **95**, 285-293. https://doi.org/10.1016/j.ajhg.2014.07.012

[5] Kaur, A., Suranagi, V., Patil, K. and Bannur, H. (2016) Neu-Laxova Syndrome: An Unusual Association with Kyphosis. *Turkish Journal of Pathology*, **34**, 259-261.

[6] Özcan, D., Derbent, M., Seçkin, D., Bikmaz, Y.E., Ağildere, M., De Sandre-Giovannoli, A. and Gürakan, B. (2013) A Collodion Baby with Facial Dysmorphism, Limb Anomalies, Pachygyria and Genital Hypoplasia: A Mild Form of Neu-Laxova Syndrome or a New Entity? *Annals of Dermatology*, **25**, 483. https://doi.org/10.5021/ad.2013.25.4.483

[7] Darouich, S., Boujelbene, N., Kehila, M., Chanoufi, M.B., Reziga, H., Gaigi, S. and Masmoudi, A. (2016) Syndrome de Neu-Laxova : rapport de trois cas et revue de la littérature. *Annales de Pathologie*, **36**, 235-244. https://doi.org/10.1016/j.annpat.2016.04.004

[8] Dwivedi, T. and Gosavi, M. (2019) Neu Laxova Syndrome. *Indian Journal of Pathology Microbiology*, **62**, 149-152. https://doi.org/10.4103/IJPM.IJPM_351_17

[9] Ficch, N., Kewh, I. and Korhon, I. (1982) The Neu-Laxova Syndrome: Comments on Syndrome Identification. *American Journal of Medical Genetics*, **13**, 445-452. https://doi.org/10.1002/ajmg.1320130415

[10] Pearl, P.L. (2017) Neu-Laxova Syndrome. http://www.rarediseases.org/rare-diseases/neu-laxova-syndrome

[11] Aslan, H., Gul, A., Polat, I., Mutaf, C., Agar, M., Ceylan, Y., *et al*. (2002) Prenatal Diagnosis of Neu-Laxova Syndrome: A Case Report. *BMC Pregnancy Childbirth*, **2**, 1. https://doi.org/10.1186/1471-2393-2-1

[12] Tarim, E. and Bolat, F. (2010) Prenatal Diagnosis and Postmortem Findings of Neu-Laxova Syndrome. *Journal of the Turkish-German Gynecological Association*, **11**, 225-227. https://doi.org/10.5152/jtgga.2010.44

[13] Williams, M.L. and Elias, P.M. (1987) Genetically Transmitted, Generalized Disorders of Cornification: The Ichthyoses. *Dermatologic Clinics*, **5**, 155-178. https://doi.org/10.1016/S0733-8635(18)30772-1

[14] Rand, R.E. and Baden, H.P. (1983) Continuing Medical Education: The Ichthyoses—A Review. *Journal of the American Academy Dermdtology*, **8**, 285-305. https://doi.org/10.1016/S0190-9622(83)80322-3