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Case Report (Pages: 93-97)

Neonatal Progeroid Syndrome (Weidman Rautenstrauch Syndrome): A Case Report from Jammu &Kashmir, Northern India

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Abstract

Neonatal Progeroid Syndrome (NPS) is a premature aging syndrome in which features of human aging are apparent at birth, including larger than normal sized head; prominent scalp veins; triangular, aged face; wrinkled skin; and decreased fat under the skin. This differentiates this syndrome from other premature aging syndromes such as Hutchinson–Gilford Progeria Syndrome (HGPS) more commonly called "progeria" in which characteristics of premature aging typically become apparent some time after birth. Although the exact cause of neonatal Progeroid Syndrome (PS) is unknown, it is believed to be genetic and inherited in an autosomal recessive fashion. Treatment is based on the individual's specific symptoms.

A female one month old with features supporting a diagnosis of neonatal progeroid syndrome: Weidman Rautenstrauch Syndrome (WRS) presented to our Neonatology Ward of GB Pant Children Hospital, Srinagar-India. She had prenatal and post natal growth failure, generalized lipoatrophy, triangular face, pseudo hydrocephalous, sparse scalp hair and eye brows, prominent scalp veins and greatly widened anterior fontanelle.

Key Words: Lipodystrophy, Neonatal Progeroid syndrome, Premature aging, Weidman Rautenstrauch syndrome.

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Introduction

The neonatal progeroid syndrome (WRS) is a very rare genetic disorder. There has been around 30 cases of WRS reported in literature. It represents complex symptoms with an unknown cause and pathogenesis (1).

It characterizes a premature aging syndrome in which several features of aging are apparent at birth therefore allowing their grouping as a neonatal progeroid condition (2). In 1977, Rautenstrauch and Snigula reported on 2 sisters with a progeria like syndrome (3). In 1979, Weidman described 2 unrelated males with same condition (4).

In 1981, Devos et al. (5) reported another child whose parents were double first cousins, and in 1988, Rudin et al. (6) reported on a single affected child. After that more patients were reported. Martin et al. (7) described neuropathological studies and suggested the WRS is a form of sudanophilic leukodystrophy. Longevity of these patients is unknown. Here we report a Kashmiri child with WRS, who presented at one month of age.

Case Report

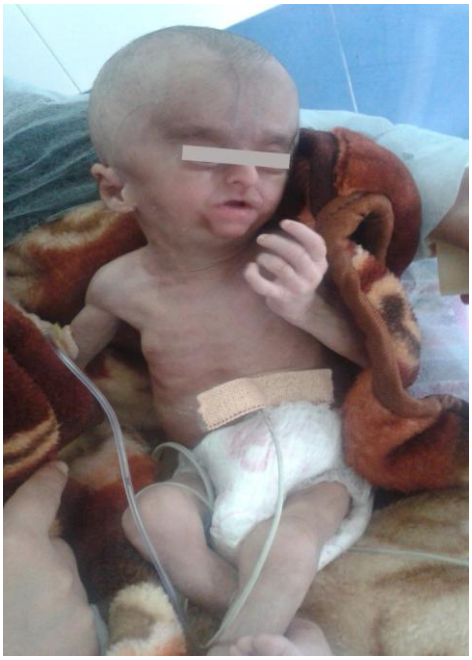
A one month old child first birth order, product of non consanguineous marriage. Pregnancy was uncomplicated with no oligohydramnios or drug intake by mother. Maternal and paternal age was 28 and 34 years respectively.

Child was born by Lower Segment Caesarean Section (LSCS) and delivery was uncomplicated. Her birth weight was 2 kg and she was full term. The patient was referred to our hospital at one month of age with decreased feeding, inadequate weight gain and abnormal facial features. There was no family history of such symptoms in family. The patient had weight of 2.1 kg, and length was 52 cm. The Occipitofrontal Circumference(OFC) was 46 cm.

The patient has craniofacial disproportion which gives a pseudo hydrocephalic appearance with wide anterior fontanelle and dry sparse scalp hair. There was prominent large fore head and visible dilated scalp veins. The face was triangular, ears were low set, sparse eye brows with long eye lashes, nasal bride was depressed and long philtrum. There was also protruding lower jaw, neck was short and both hands and feet were relatively large with long fingers and toes with loss of subcutaneous fat over them. There was generalized lipoatrophy all over the body.

Chest examinations was normal. Cardiac examination revealed grade 3 systolic murmur best heard in left second and third intercostals space. By inspection of abdomen there was generalized bulge with apparent lobulation on the anterior abdominal wall (mostly distended loops of intestine). Umbilicus was shifted downward a flat.

Neurological examination was normal. Echocardiography was suggestive of small Patent Ductus Arteriosus (PDA). Abdominal Ultrasonography (USG) was normal. Complete blood picture was normal apart from low hemoglobin level (7.8g/dl), serum ca phosphorous and alkaline phosphatases were normal. Thyroid profile was also normal. Computerized Tomography (CT scan) and Magnetic Resonance Imaging (MRI) brain did not revealed any abnormality.



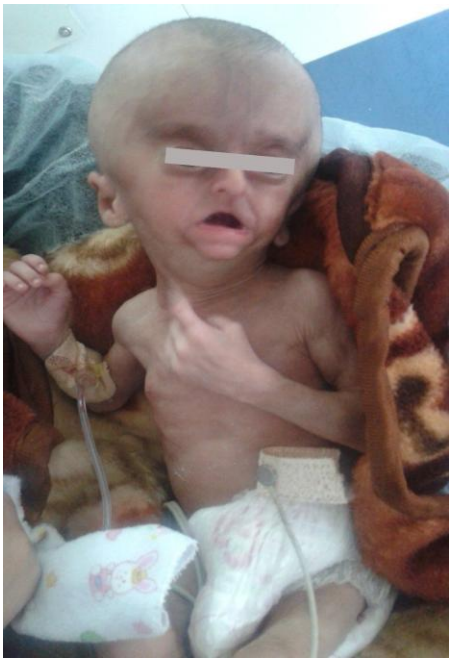


Fig.1 **Fig.2**

Fig.1 & 2: Showing craniofacial disproportion, pseudo hydrocephalic appearance, sparse scalp hair, visible dilated scalp veins and absence of subcutaneous fat.

Discussion

We report a one month old child with features of premature aging in favor of diagnosis of WRS. These features included intrauterine and post natal growth failure and old looking face, psedo hydrocephalous, craniofacial disproportion large anterior fontanelle, prominent scalp veins, sparse scalp hair and eyebrows sunken eyes, low set ears, marked reduced subcutaneous fat and relatively large feet and hands. The same features were reported previously (4-9). In our patient the abdomen appeared large and prominent as was reported earlier (10).

However some characteristic features reported in WRS patients are missing in our patient like presence of neonatal teeth which is considered very helpful in diagnosis (3-5). However neonatal teeth were not reported in a Turkish patient and in other 19 published cases. Feeding difficulties reported in many patients with WRS (7) were not reported in our patient where in spite of high caloric nutrition, the increase in weight was not satisfactory and she was underweight and anemic. Skeletal findings reported in some WRS patients including scoliosis characteristics of a neuromuscular curve (15), osteoporosis with loose joints, camptodactyly, joint contracture (11), and congenital hip dysplasia (16) were not reported in our patient. However our patient should be followed up regularly as these findings may represent progression.

Ocular manifestations include, cloudy cornea with congenital glaucoma, other dermatological manifestations like dermatitis acrodermatitis enteropathica reported in some patients (14) were not reported in our patient. Microstomia as reported with WRS (3) and (13) was also reported in our patient. Also our patient had small maxilla. Computed Tomography (CT) findings like Dandy walker cyst and ventriculomegaly, basal ganglia calcification reported in

some patients (11) and agenesis of corpus callosum reported in other patients (16) were not reported in our patient. Patients with WRS usually have short life expectations (15) the disease is usually lethal by 7 months however some have reported survival of patients up to teens and 20s (18). Our patient was the product of non consanguineous marriage. However Arboleda et al. (2) reported it in parents with consanguineous marriage supporting its autosomal inheritance. The etiology of WRS remains unknown. Several studies analyzing telomere length and lamin A gene had not revealed any alterations. However, mutations in LMNA gene had been reported in several other atypical progeroid syndromes. Based on these observations, several hypotheses could be withdrawn concerning the etiology of WRS. The study of genes associated with lamin A metabolism, such as ZMPSTE24, and the metabolic pathways associated with insulin, such as protein kinase B or AKT, are of particular interest. WRS characteristic were believed to indicate that the discovery of the gene and the metabolic pathway associated with this syndrome will most likely lead to new knowledge about the physiopathology of human aging (2). However mutations in Lamin A/C (LMNA) gene were not found in four WRS patients, and in particular, G608G mutation (GGC > GGT transition) which is associated with most cases of Hutchinson Gilford progeria (OMIM:176670). These findings suggest that WRS represents a distinct progeroid entity that may be caused by recessive mutations of a different gene (20).

Increased chromosomal breakage and the presence of basal ganglia calcification after early childhood suggest that DNA repair defects are involved in the pathogenesis of this disorder. LMNA, ERCC8, or ZMPSTE24 gene mutations could not account for the disorders in these patients. Thus this rare disorder represents a complex of symptoms with unknown cause and pathogenesis, and more than one disease may account for the clinical variability of WRS (11). Terminal Restriction Fragment (TRF) length to evaluate whether the patient's premature aging process is accompanied by shortening of telomere length in her cultured fibroblasts was studied. Mean TRF of 13.5 kb found in the patient's fibroblasts was not shortened as compared to that of normalfibroblasts. These results differ from those observed in Hutch-inson Gilford progeria. Jager et al. (21) reported that lackof cellular differentiation capacity in WRS patients may be responsible for the clinical appearance and symptoms of this rare disorder. Karyotype was normal in patients with WRS(11) as was found in our patient. Ultrasound examination can be a useful tool in prenatal diagnosis of this rare syndrome. During pregnancy growth retardation particularly in the biparietal diameter and abdominal diameters but not in the femoral length can be detected through serial ultrasound scans (12).

To conclude WRS represents a complex of symptoms and signs with an unknown cause and pathogenesis. Variability in the phenotype of WRS is clear, however the phenotype remains distinct enough to allow a secure diagnosis (13). This case is a contribution to the exact description of that extremely rare syndrome. We hope to facilitate establishing the major and minor criteria to help the differential diagnosis in difficult cases because of heterogeneity. We have to discuss if the WRS really represents a separate genetic entity within the group of premature aging syndromes. Long term follow up of patients with WRS should provide information relative to their ultimate psychomotor development.

Conflict of interests: None.

Aknowledgement

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