CASE REPORT

A Newborn with Icthyosis, Corpus Callosum Hypoplasia, Microcephaly, Atrichia and Intra Uterine Growth Retardation (IUGR): A Variant of Icthyosis Follicularis Atrichia Photophobia (IFAP) or Brain Anomalies, Retardation, Ectodermal Dysplasia, Skeletal Deformities, Hirschsprung Disease, Ear/Eye Anomalies, Cleft Palate, Cryptorchidism (BRESHECK)?

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Abstract:

A full term newborn small for gestational age Intra Uterine Growth Retardation (IUGR) admitted with congenital dysmorphic features with icthyosis, atrichia, microcephaly and eye abnormalities, when explored further for other congenital malformations, revealed Corpus callosum hypoplasia and closely related features with two rare syndromes Icthyosis Follicularis Atrichia Photophobia (IFAP) or Brain Anomalies Retardation, Ectodermal Dysplasia, Skeletal Deformities, Hirschsprung Disease, Hemivertebrae, Ear/Eye Anomalies, and Kidney Dysplasia (BRESHECK).

Keywords: Newborn, Anomaly, IFAP, BRESHECK

Introduction:

A newborn with different congenital malformations encompasses variants of syndromes and with overlapping signs. They are solely diagnosed sometimes based either only on clinical features or additionally with confirmatory laboratory investigations. A new born is presented with features of icthyosis, intra uterine growth retardation, microcephaly alopecia absent eyebrows and eyelashes, cleft palate and cerebral corpus callosum hypoplasia. These features were intersection of two syndromes namely, Icthyosis Follicularis Atrichia Photophobia (IFAP) and Brain Anomalies Retardation, Ectodermal Dysplasia, Skeletal Deformities, Hirschsprung Disease, Hemivertebrae, Ear/Eye Anomalies, and Kidney Dysplasia (BRESHECK).

Case Report:

A 23 year non consanguineous, third gravida mother with history of oligohydramnios and one abortion delivered a full term male new born, weighing 1.750 kg , with severe Intra Uterine Growth Retardation (IUGR), uncomplicated breech vaginal delivery which was admitted in Neonatal Intensive Care Unit on 05/06/2017. On physical examination head circumference was 30 cm, chest circumference 26.5 cm, length was 42 cm, whole body was covered with collodion and icthyosis (Fig.1) associated with microcephaly, intrauterine growth retardation, total alopecia, low set ears, proptosis of eyes, absence of eyebrows and eyelashes, (Fig. 2), cleft palate, short neck, simian crease, cryptorchidism and micropenis. On systemic examination, a pansystolic murmur in the left parasternal area was present, later tonic posturing of both upper limb developed gradually after birth. Anemia, tachycardia and mild congestive failure which appeared later responded to diuretics and packed cell transfusion. Septicemia was treated with antibiotics. Antenatal

ultrasonography revealed oligohydramnios, hydrocephalus and grossly dilated ventricles. Toxoplasma, HIV, syphilis, rubella, cyto-megalovirus, herpes infections were ruled out. In initial blood reports, hemoglobin was 14.3, total leukocyte count 28000, platelet count 185000, C-reactive protein was normal, however later, total leukocyte counts 39000, platelet count 90000 and C-reactive protein became positive (2.4 mg/dl), patient had septicemia, though blood culture was negative. Liver and kidney function tests and serum electrolytes were normal. Consultation of skin specialist and ophthalmologist was sought which revealed ichthyosis and right eyemadarosis, normal fundus and bilateral disc pallor respectively. On X-ray chest cardiomegaly was present X ray spine had multiple hemivertebrae (Fig.3) in thoracic and lumbar regions. Ultra-sonography (USG) skull detected asymmetrical dilatation of both lateral ventricles with rounded cystic lesion in left lateral ventricle, well defined cystic lesion with internal echoes in the vicinity of right lateral ventricle with hemorrhage and absence of corpus callosum. In USG, abdomen and external genitalia cryptorchidism was detected. Large ventricular septal defect with atrial septal defect was detected on 2D echocardiography CT scan (without contrast) a hemorrhage and dilatation was noted in velum interposition extending into cysterna magna, frontal horn and anterior body of both lateral ventricle (Fig. 4) with compressive displacement of temporal, occipital horns and posterior body of both lateral ventricles suggesting further for Magnetic Resonance Imagining (MRI) in which splenium of corpus callosum being hypoplastic and paucity of parieto-occipital white matter, and a internal encepha-locele herniating into uppercervical canal was seen. A normal karyotyping was reported in this case. The newborn had septicemia with pneumonia and therefore was put on ventilator and i.v. antibiotics, but the patient expired.

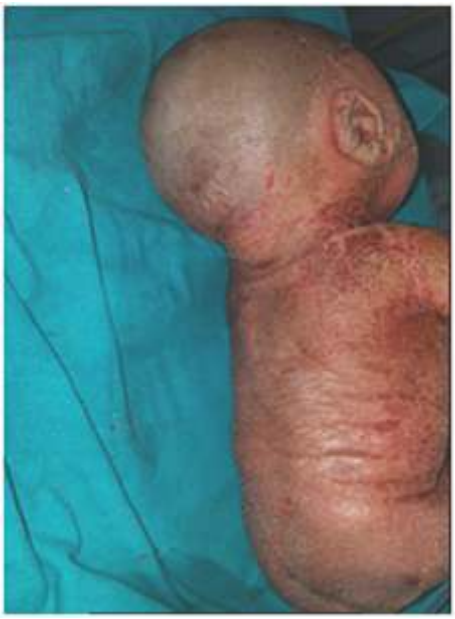

Fig. 1: Whole Body Icthyosis

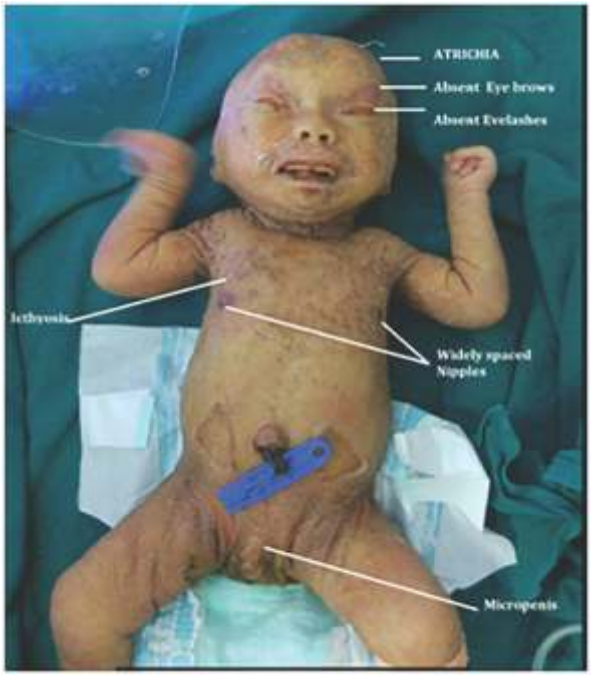

Fig. 2: Total Alopecia (Atrichia), Absence of Eye brows and Eyelashes

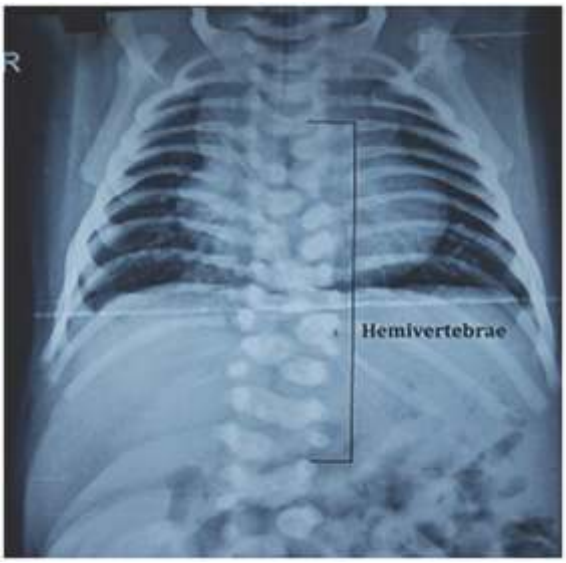

Fig. 3: Hemivertebrae

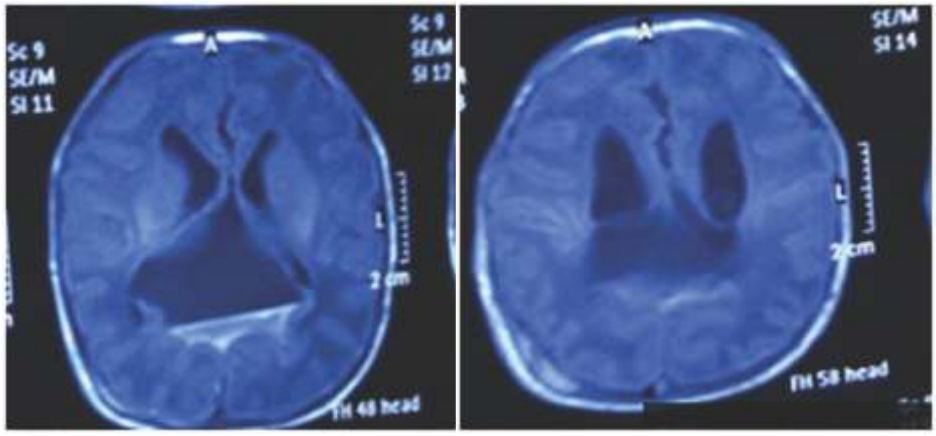

Fig. 4: Dilated Ventricles with Hemorrhage on Contrast

Discussion:

A search for newborn with similar antenatal history, dysmorphic clinical features and investigations in this case report was corroborated in literature and text. Two rare syndromes correlating with maximum similar features were found one was IFAP other with additional features, acronym as BRESHECK. There are up to 40 cases of IFAP and only five to six cases of BRESHECK syndrome are reported so far. The syndrome of IFAP was first reported by McLeod [1] in 1909 with features of severe follicular hyperkeratosis on scalp extensor surfaces of limbs and complete baldness, this keratotic lesions did not appear before the age of 2 yr Congenital alopecia is a distinct clinical finding which typically involves scalp, eyebrows and eyelashes. Features of follicularicthyosis, alopecia and photophobia in 2 boys were observed by Zeligman and Fisher [2] in

1959, same features were also observed by Eramo *et al*. [3] in 1985. The manifestations of IFAP syndrome had additional features with mental retardation seizures, generalized alopecia, hypohydrosis, vertebral and renal anomalies, chromosomal analysis being normal. Features of IFAP syndrome were common with another closely related subset described as BRESEK by Reish *et al*. [4] (Brain anomalies, retardation, ectodermal dysplasia, skeletal anomalies, eye/ear and kidney anomalies, with additional features Hirscsprungmegacolon and cryptorchidism described above as BRESHECK. In the current case renal anomalies or congenital megacolon were not detected. Cytogenetic studies (karyotyping) was normal as in other cases. A Japanese boy with multiple severe congenital anomalies consistent with BRESHECK including hemivertebrae with desqamated skin was reported by Naiki *et al.* [5], Brain MRI at the age of 3 year showed decreased volumes of frontal and parietal lobes, thinning of corpus callosum and ventricular dilatation. Some of the above signs are present in females (being a carrier) up to certain extent such as skin and hair manifestations. Thus most of the features described in BRESHECK syndrome were present in current case. However, photophobia could not be appreciated (which may appear until later in childhood in some cases) or due to proptosis. Congenital VSD with ASD was an additional finding in our case. As far as genetics of IFAP and BRESHECK syndrome is concerned, it is an X -linked recessive disorder with mutations in MBTPS2 at least in patients considered to have the BRESHECK condition, MBTPS2 is a membrane embedded zinc metalloprotease that activates signaling metalloprotease that activates signaling proteins involved in sterol control of transcription and endoplasmic reticulum stress. Mutations that lead to lowest residual activity of MBTPS2 had severely affected phenotypes [6-8]. Activity has been shown to vary with different mutations hence there is a possibility that all cases of IFAP with or without added BRESHECK findings are of a clinical spectrum of a single disorder with variable expressivity.

Conclusion:

Clinical skin manifestations such as atrichia present in a newborn at birth should be evaluated for Nervous system anomalies or defects also as both the systems share common embryogenesis from ectoderm and may help in identifying variants of rare syndromes like IFAP or BRESHECK.

References

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