CASE REPORT

Lenz majewskihyperostotic dwarfism: A Pakistani patient with atypical features

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Abstract

Lenz-Majewski Hyperostotic Dwarfism (LMHD) is an extremely rare congenital, sclerosing bone dysplasia that causes cranio-tubular hyperostosis, ectodermal dysplasia (cutis laxa and enamel hypoplasia), osseous dysgenesis of hands and feet with diaphyseal cortical thickening of tubular bones and intellectual disability. Only a few cases of this syndrome have been reported in the literature so far. We report another case of LMHD with cranio-tubular hyperostosis, cutis laxa, wide open anterior and posterior fontannels, hypertelorism and thickening of diaphysis of tubular bones in a six months old Pakistani female patient. Notably, some secondary phenotypic clinical features such as multiple bony deformities, multiple skin tags and a space occupying lesion in posterior cranial fossa (Lipoma) resulting in obstructive hydrocephalus were also present in this patient. These atypical features have never been previously reported with LMHD, to the best of our knowledge. This case extends the variable phenotype and associated features of this syndrome.

Keywords: Lenz-Majewski Hyperostotic Dwarfism, Lipoma, Obstructive Hydrocephalus.

Introduction

Lenz Majewski Hyperostotic Dwarfism (LMHD) was first described by Braham RL, in 1969, in a paediatric patient with several clinical features identical to Camurati-Engleman syndrome, another hyperostotic disorder associated with unusual features of progeria, widened ribs, enamel dysplasia, webbed hands and brachysyndactyly.[1] Another paediatric patient with strikingly similar characteristics of progeria, enamel hypoplasia, craniodiaphyseal hyperostosis, choanal atresia and symphalangism, was later reported by Lenz and Majewski.[2] These malformations were subsequently compiled into a distinct entity, LMHD. Some recent studies have linked the occurrence of LMHD to PTDSS1 gene that encodes Phosphatidylserine synthase 1 (PSS1). These studies confirm that a heterozygous gain of function (missense) mutation in PTDSS1 gene causes LMHD.[3] Only a few cases have been reported.[4-6] These cases were sporadic in nature with some evidence pointing to advanced paternal age.

Herein we describe an additional patient of LMHD having both, classical and atypical features, which may add to the clinical spectrum of this phenotypically variable disorder. The cause of obstructive hydrocephalus has specifically been emphasized.

Case Report

This case presented at Department of Pediatrics Unit II, Civil Hospital Karachi, Pakistan in January, 2017. A six-months old female baby, third product of a consanguineous marriage was born to a family of 30 year old mother and 37 year old father with insignificant family history, at 38th week of gestation via normal vaginal delivery. There was a history of polyhydramnios on antenatal ultrasonography. She weighed 2.5 kg, was 48 cm in length, and had an occipitofrontal circumference (OFC) of 34 cm at birth. Baby was born with a short neck, thin lax skin with wrinkles over the spine and multiple skin tags. Multiple bony deformities were noticed at birth involving both forearms, hands and right foot. She had failure to thrive. Developmental delay was present such as achieving social smile at 4 months and being unable to recognize her mother and not able to hold her neck till six months.

Examination revealed an infant with below average physique having a weight of 5.5 kg (below 50th centile), length of 62 cm (below 50th centile) and OFC of 42.5 cm (between 50th and 75th centile). The head was relatively large with frontal bossing, anterior and posterior fontannels were wide open and bulging. Hypertelorism of otherwise normal eyes and low set ears were noted. Nose, mouth and chin were found to be normal. Neck appeared short with lax skin on the posterior side. Laxity in skin was observed all over the body, particularly over mid abdomen and on back covering spine with multiple wrinkles extending from neck downwards till anus. Multiple skin tags were present; two large tags on the anterior chest, one small tag on right forearm, two small tags around the anus, largest measuring 2.5 cm and smallest being 0.5 cm with normal overlying skin. Both forearms were relatively short with deformities.

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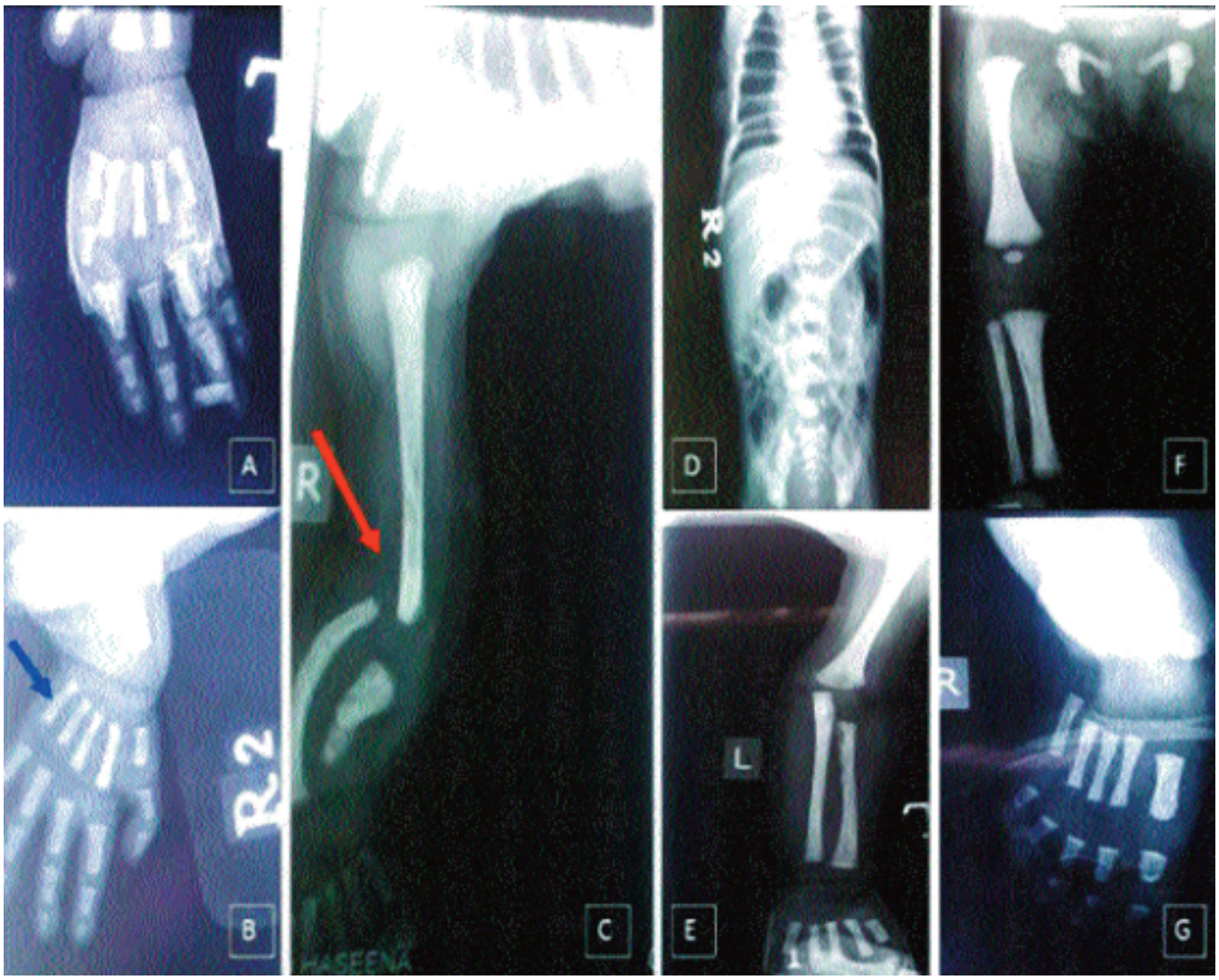

Figure-1: (A-G) Generalized increase in bone density was noted in all X-rays. X-ray of right forearm and hand revealed short and deformed radius and ulna (red arrow) and short right 5th metacarpal bone (blue arrow).

Both hands also revealed deformities. There was an outward deviation of the right foot. Central nervous system (CNS) examination showed increased tone in all four limbs with brisk reflexes and sustained clonus. Signs of raised intra cranial pressure (ICP) and meningeal irritation were absent. Examination of chest and abdomen was unremarkable. Radiology of skull, chest, abdomen and all four limbs was carried out. Generalized increase in bone density was noted in all x-rays. X-ray of skull ruled out the possibility of choanal atresia. X-ray of right forearm and hand revealed short and deformed radius and ulna and short right 5th metacarpal bone (Figure-1). Ultrasonography of abdomen and echocardiography did not reveal any abnormality.

MRI brain with contrast was done. Marked cortical atrophy with prominent sulci and extra cerebral CSF spaces were noted. Gross dilatation of both lateral ventricles and 3rd ventricle was noticed with evidence of focal space occupying lesion in posterior fossa extending down into cervical canal causing obstructive hydrocephalus (Figure-2).

For the multi-disciplinary management of the patient, department of neurosurgery, orthopaedics and dermatology were consulted and the patient was managed accordingly.

Formal informed and written consent was taken from the patient's parents prior to the reporting of the case.

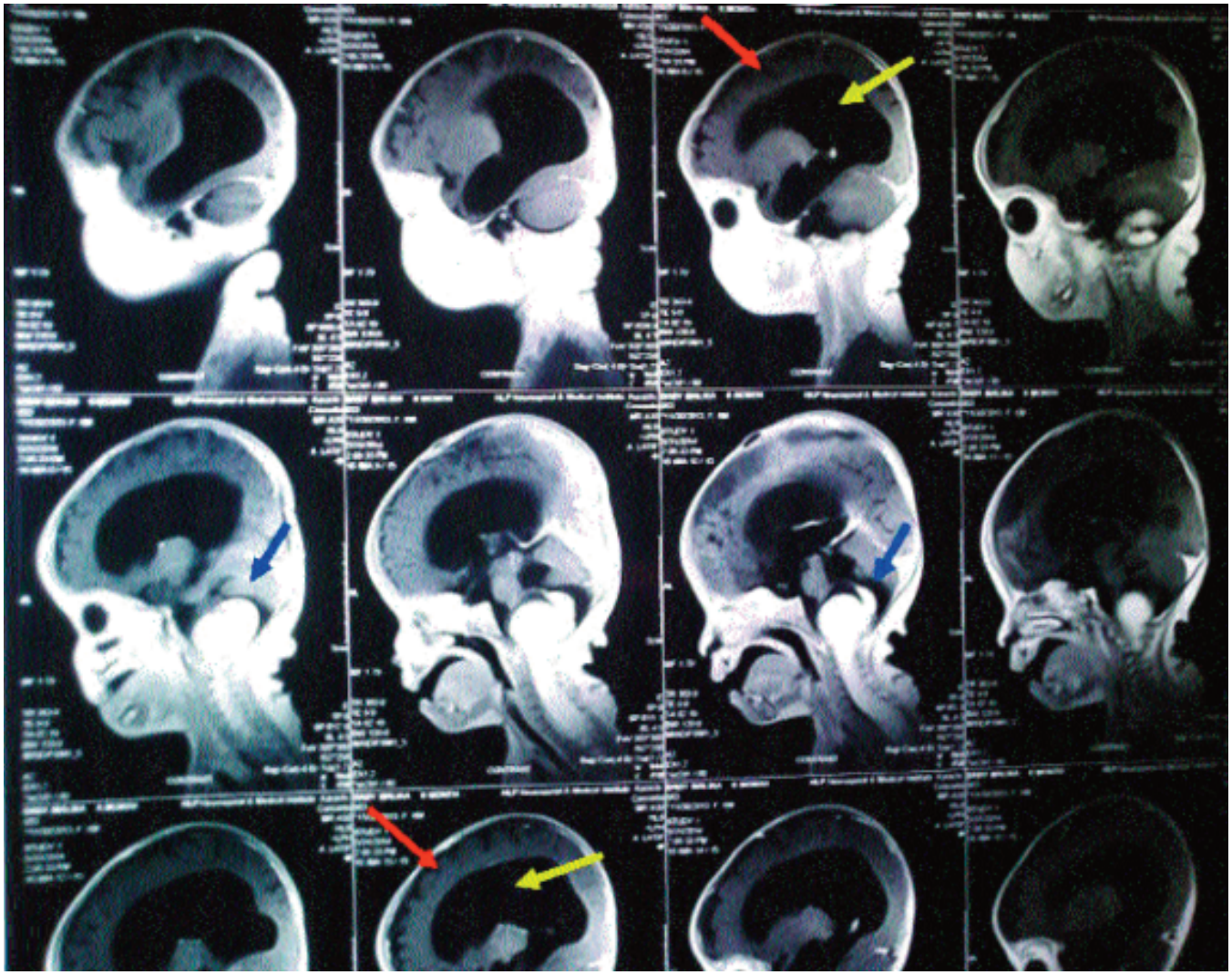

Figure-2: An MRI brain with contrast showing marked cortical atrophy (red arrow), gross dilation of lateral and 3rd ventricles (yellow arrow), space occupying lesion (lipoma) in the posterior cranial fossa (blue arrow) extending into the cervical canal causing obstructive hydrocephalus.

Discussion

LMHD is a distinct form of craniotubular bone disorder characterized by disproportionately large head, craniotubular hyperostosis with wide open fontannels and delayed closure of sutures, ectodermal dysplasia that includes loose, atrophic/wrinkled skin with prominent veins on the scalp (Cutis laxa) and enamel hypolasia, brachymesophalangy with proximal symphalangism. Webbed fingers and toes, large floppy ears, choanal atresia, nasolacrimal duct obstruction, cryptorchidism and inguinal hernia are some of the other frequent clinical findings. Mental retardation with low IQ levels and failure to thrive are also often observed. Radiographic features of syndrome include osteosclerosis of skull, vertebra and facial bones, broad ribs and clavicle, short or absent middle phalanges and defective skeletal maturation.[7]

The 2006 revised version of Nosology and Classification of Genetic Skeletal Disorders includes this disorder (along with Camurati- Engelmann, craniometaphyseal dysplasia, craniodiaphyscal dysplasia, Pachydermoperiostosis, and so on.) under the category of increased bone thickness with metaphyseal and/or diaphyseal involvement.[8] Recently, the genetic basis of LMHD has been discovered. It has been established that a mutation in PTDSS1 gene, mapped to chromosome 8q22 that encodes Phosphatidylserine synthase (PSS1) causes this disorder.[3] This case describes an infant with LMHD who has both the classical and non-classical features of the syndrome.

Findings of developmental delay, failure to thrive, large

head with frontal bossing, wide open fontannels, hypertelorism of the eyes, short neck with thin lax skin and skeletal abnormalities are the features consistent with other cases of Lenz-Majewski syndrome described in literature. However, multiple bony deformities, skin tags and posterior fossa lipoma causing obstructive hydrocephalus have never been reported till date suggesting that they can be included as atypical features of this disease.

The skeletal changes of Lenz-Majewski syndrome previously reported, comprise of progressive hyperostosis of craniofacial bones, cortical thickening of diaphysis of tubular bones and brachymesophalangy with proximal symphalangism. In addition to these, our patient also presented with deformities of multiple bones (including short and deformed radius and ulna, short 5th metacarpal and deformed foot) and atypical skin tags involving the area of chest, forearm and anus. Hydrocephalus in patients with LMHD has been reported twice previously by Wattanasirichaigoona et al[9] and Shoja et al.[10] In a patient with communicating hydrocephalus, Wattanasirichaigoon et al, reported a decent response to carbonic anhydrase inhibitor, and attributed the cause of hydrocephalus to an attenuation of inferior sigmoid sinuses and jugular bulbs which may interfere with absorption of CSF and cause impaired intracranial venous drainage while Shoja et al, suggested narrowing of foramen magnum as a possible cause of hydrocephalus. Gorlin and Whitley also reported mild dilation of lateral ventricles in their patient without manifestation of intracranial hypertension.[7]

In our case, an MRI brain with contrast revealed a mass lesion in posterior cranial fossa (possibly lipoma) which could be a potential cause of obstructive hydrocephalus. This association between posterior cranial fossa mass and subsequent development of hydrocephalus is unique and another atypical feature of LMHD.

Lenz-Majewski syndrome is a rare condition and the existent literature demonstrates a variable and extensive heterozygous phenotypic presentation of the syndrome. This case agrees with previous reports and further extends the phenotypic variability associated with this syndrome.

Disclaimer: The abstract has not been presented or published in any journal or conference.

Consent: Informed consent was obtained from the patient's parents prior to the reporting of the case.

Conflict of Interest: The person who issued the ethical approval is also a co-author of this case report.

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