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Original Research Paper

Radiodiagnosis

FEMORAL-FACIAL SYNDROME - A RARE CASE REPORT

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ABSTRACT Femoral-facial syndrome (FFS) is an extremely rare fetal malformation. It comprises bilateral femoral hypoplasia and craniofacial dysmorphism. Maternal diabetes is associated with approximately 40% of cases of FFS. We present the case of Femoral-Facial syndrome of Newborn female child. She was delivered by vaginal route at 36th week of gestation. Mother had a history of type 2 diabetes mellitus. She was having markedly shortened bilateral lower limbs, deformed hip joint and mild talipes equino-varus deformity of left foot. There was prominent forehead, short nose with broad tip, long philthrum, thin upper lip, micrognathism and malformed low set external ears. Skeletal radiograph shows complete absence of right femur and marked hypoplasia of left femur.

KEYWORDS : Diabetes, Femoral-facial syndrome, Skeletal radiograph

INTRODUCTION

Femoral-facial syndrome (FFS) is an extremely rare fetal malformation of unknown etiology. It comprises bilateral femoral hypoplasia and craniofacial dysmorphism with cleft palate, thin upper lip, micrognathia, flat philtrum, short nose with broad tip and upslanting palpebral fissure.[1,2] Other findings include hypoplasia of fibulae, club foot, lumbar spine and pelvic anomalies. Other systemic anomalies such as cardiovascular and genitourinary anomalies may be associated with limb defects. The two principal characteristics of this syndrome, micrognathia and shortened femur, can be demonstrated by sonographic (US) imaging in the early stages of pregnancy. Despite this, it has rarely been reported in the first trimester.[3,4] It was first described by Daentt et al.[5] in 1975 and is more common in females.[1] An association has been established between FFS and insulin-dependent diabetes mellitus. About 38% of affected infants are born to patients with diabetes.[6] The femoral hypoplasia unusual facies syndrome is a rarely considered clinical entity that has a strong association with maternal diabetes.[7]

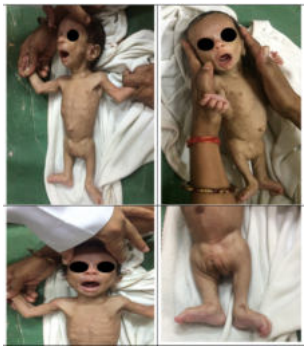
Etiopathogenesis of the syndrome is still unknown.[8] We describe here a case Femoral-Facial syndrome and the spectrum of associated malformations.

CASE REPORT

We present the case of Femoral-Facial syndrome of Newborn female girl. She was a 3rd born child of healthy non-consanguineous parents, delivered by vaginal route at 36th week of gestation presented with shortened bilateral lower limbs and unusual facies. Mother had a history of type 2 diabetes mellitus. Maternal glycohemoglobin (HbA1c) after delivery was 6.7% which was indicative of unbalanced diabetes. There was no history of teratogenic drug intake or exposure to TORCH agents. Similar complains in her siblings were not observed.

On gross physical examination of limbs, it was found that child was phenotypically female. She was having markedly shortened bilateral lower limbs, deformed hip joint and mild talipes equino-varus deformity of left foot. There were no defined knee joints. Bilateral upper limbs were normal. Gross clinical deformity of chest and abdomen was not observed. There was prominent forehead, short nose with broad tip, long philthrum, thin upper lip, micrognathism and malformed low set external ears. There was no evidence of facial clefts. These findings were suggestive of cranio-facial dysmorphism.

Figure 2: Gross Physical Examination



Patient was referred to radiodiagnosis department for skeletal radiography and ultrasonography.

Skeletal radiograph

Skeletal radiograph shows complete absence of right femur and marked hypoplasia of left femur which was consists of only small bony fragment. Bones of bilateral legs and feet were normal. Survey of the rest of the skeleton didn't reveal any bony abnormality. Ultrasound of abdomen and echocardiography were normal.

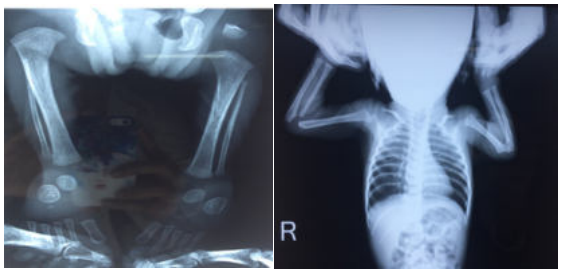


Figure 1: Skeletal radiographs

DISCUSSION

The variability of the clinical expression and severity of FFS is emphasized in the literature. The case described in this report fit well with the moderate to severe end of the clinical spectrum

of FFS. The present case presented with extreme shortening of lower limbs, deformed hip joint and mild talipes equino-varus deformity. There were no defined knee joints. In addition to the characteristic facial dysmorphism, femoral hypoplasia, and severe hypoplastic external genitalia. In the previous literature, the characteristics of facial dysmorphism was variable, ranging from evident Pierre Robin sequence to subtle features such as upslanting palpebral fissures, long philtrum, short broad-tipped nose, cleft palate, thin lips, and micrognathia.[3,9,10] The most common facial feature is micrognathia (75%). The femoral involvement can be unilateral and of a variable degree, ranging from femoral agenesis to mild hypoplasia.[3,4,10] In addition to skeletal and craniofacial anomalies, other visceral abnormalities such as genitourinary, cardiovascular, CNS systems may be involved. Absence of the femur is a rare finding in FFS.[8]

Prenatal diagnosis suspicion of FFS is easy by ultrasound since the major abnormalities can be detected in utero in either late first or early second trimester, especially in the setting of maternal diabetes. The 2 major signs, which can lead to the consideration of FFS, are the extremely- shortened or absent femora and the severe micrognathia.[3,4] Prenatal ultrasound was not performed in our case. Early diagnosis is of extremely great importance as it allows providing parents with the necessary information about the evolution and prognosis of this syndrome.

The differential diagnosis of FFS involves a group of rare diseases whose characteristic features include micrognathia and femoral hypoplasia, especially skeletal dysplasias such as campomelic dysplasia, Antley-Bixler syndrome, and kyphomelic dysplasia. In fact, these conditions are characterized by shortening and abnormal bowing of the long bones. In FFS, the femora are usually more severely affected and the other long bones are rarely involved. The CRS should also be considered in the differential diagnosis. There are many findings which overlap between CRS & FFS, especially the sacral and urogenital tract abnormalities, though facial anomalies are uncommon in CRS and the sacral dysgenesis is less frequently observed in FFS. Given their similarities, both conditions may represent different manifestations of the same disorder which is relevant to a common pathogenetic mechanism affecting the early skeletal morphogenesis at different times of embryogenesis,[2,7,10] The report of Gupta et al.[11] of an infant born to diabetic mother and presenting with features of both disorders supports this hypothesis.

The etiology of this syndrome has remained uncertain.[5] Maternal diabetes is associated with approximately 40% of cases of FFS. Malformation includes neural tube defects, caudal dysgenesis, congenital heart defects, vertebral defects, femoral hypoplasia and renal anomalies in infants of diabetic mothers.[6] The caudal dysplasia syndrome and FH-UFS have been reported to be more frequent among infants of diabetic mothers.[12]

The risk of this disease could be increased by interaction of maternal diabetes with genetic factors. Genetic involvement is early aroused by Lampert et al.[13] who describes an affected father and daughter and suggests that FFS may be inherited as an autosomal dominant trait.

The report of Robinow et al.[14] also supports the occasional transmission of the FFS as an autosomal dominant with incomplete penetrance. It is plausible to suggest that disturbance of glucose pathways in early development, similar to other teratogens such as viral infection, perfusion failure, and drug exposure, would be a strong maternal environmental factor acting on a polygenic background. Thus FFS is a condition that underlies complex and multifactorial mechanisms rather than a syndromic entity resulting from a simple genetic mechanism. The recent report of Spielmann et al. provides a powerful argument in favor of a genetic basis of FFS. Using a combination of array CGH, qPCR, and FISH, they identified a de novo deletion/duplication together encompassing more than 70 genes in terminal 2q in an affected girl born to nondiabetic mother. The size, gene content, and de novo occurrence of this chromosome abnormality provide consistent evidence of its pathogenicity. These findings corroborate the hypothesis of a polygenic background, but do not exclude a multifactorial pathogenesis.

CONCLUSION

Above mentioned case report fits into the classical clinical spectrum of femoral hypoplasia- unusual facies syndrome. The possible etiopathogenensis of the syndrome still remains unknown, but the possible teratogenic potential of maternal diabetes might be an attributable risk factor. The fetopathologic examination allowed us to especially point out the variable expression of this challenging condition and the significant abnormalities in femoral growth plate. These findings emphasize the need for etiologic investigation of FFS that shows multifactorial inheritance.

DECLARATIONS

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