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Case Report

Fetal Varicella Syndrome - A case report

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Abstract

Fetal varicella syndrome is a rare condition of the newborn, presenting with cutaneous scars, limb defects, ocular and central nervous system abnormalities. It is due to varicella or zoster developing in the fetus following maternal varicella infection during early pregnancy. We are reporting a case of congenital varicella syndrome following maternal varicella during the 17th week of pregnancy. At birth, the newborn showed haemorregic and necrotic bullae on the skin along with a linear, depressed, erythematous scars over both lower limbs that healed later with characteristic scars. In view of the risk of serious malformations following intrauterine varicella infection attempts should be made to prevent varicella zoster virus infection during pregnancy.

Key words: Congenital Varicella Syndrome, Congenital malformation, Skin lesions

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Introduction

Fetal varicella syndrome (FVS) is a rare complication of maternal varicella infection occurring in about 2% of the babies born to women infected with varicella between 7 and 28 weeks of pregnancy [1-3]. To date, nearly 100 infants born with signs of FVS have been reported in the literature. The typical clinical features include low birth weight(LBW), cutaneous lesions like scars often in a dermatomal outline (70%), papular lesions resembling connective tissue nevi, ocular abnormalities (66%) like choreoretinitis, cataracts, microophthalmia, Horner's syndrome, nystagmus, limb hypoplasia (50%), CNS abnormalities (46%) including seizures, mental retardation, hydrocephalus, cortical atrophy, cerebellar aplasia, encephalomyelitis and dorsal radiculitis, and poor sphincter control (32%) [4]. About 30% of infants born with these lesions die during the first months of life. The diagnosis of FVS should be established by the appearance of maternal varicella, the presence of typical clinical symptoms as well as the laboratory evidence of in utero varicella-zoster virus (VZV) infection. In the reviewed infants, intrauterine VZV-infection has been proved in about 60%. Passive immunization may reduce the risk of fetal infection but there is no evidence to prevent fetal viremia. Up to now, there are no controlled studies concerning antiviral chemotherapy in preventing FVS. We are reporting one such case in view of paucity of reports from the Indian subcontinent [5].

Case Report

A 2 days old female neonate born out of non-consanguineous marriage by normal vaginal delivery at term to a primigra vida with a history of chicken pox during the 17th week of pregnancy presented with an extensive vesiculobullous lesions along with scarring over the both lower limbs since birth. Birth weight of the child was 800 gms (LBW). Ultrasonography or TORCH battery could not be performed as the mother did not get routine antenatal check-ups in our hospital.

On examination the child revealed linear, irregular, depressed, erythematous scar along with vesiculobullous lesions measuring 12 cm × 5 cm over the anteromedial aspect of the both lower limbs. A similar bullous lesion was present over the abdomen and hand [Figure 1] and [Figure 2]. This distribution corresponds to L4, L5 and S1 dermatomes. There was limb hypoplasia, malformed digits, microcephaly (OFC 27cm).

Ophthalmology evaluation, neurosonogram and laboratory reports were normal.Venereal Diseases Research Laboratory test and human immunodeficiency virus anti-

bodies were non-reactive. Differential diagnosis of neonatal scars was considered, but a diagnosis of FVS was made based on the characteristic history and clinical features. The parents of the baby were counselled about the condition and reassured . No active intervention was advised at this stage. During follow up child had convulsions and gross developmental delay. Anti epileptics were started along with physiotherapy and regular follow-up.

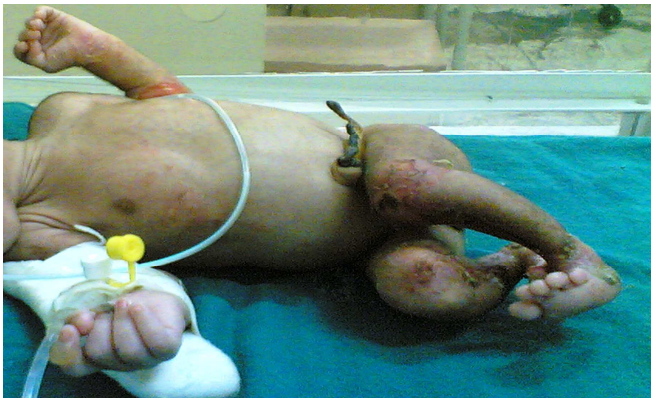

Figure 1*.Irregular, depressed, erythematous scars over hand,, abdomen and both lower limbs*

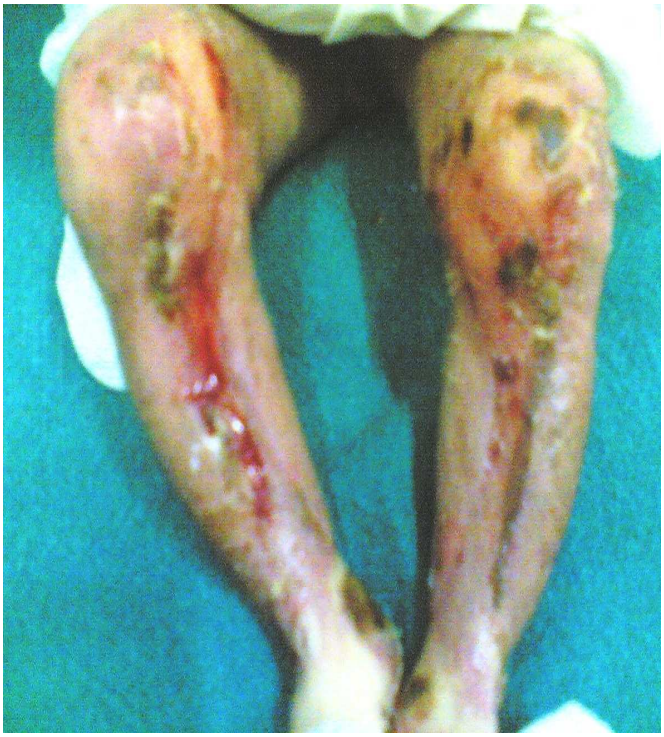

Figure 2*. Irregular, depressed, erythematous scars over both lower limbs*

Discussion

Chicken pox may develop in one to five per 10,000 pregnancies resulting into potential consequences of maternal varicella infection during pregnancy [2,4,6]. Maternal varicella during pregnancy may become more common in the future [7,8]. Over the past two decades an increasing frequency of varicella in adults in England and Wales has been reported [8]. Recent upward shift in the age distribution of varicella has been reported in the United States as well [9]. Reasons for such changes in age distribution are complex but they could herald an increased frequency of pregnant women with varicella.

FVS was first described in 1947 by La Foret and Lynch [1]. Srabstein *et al*. rediscovered the syndrome in 1974 and named it "congenital varicella syndrome" [4,10]. Subsequently, the condition has been reported under various names like congenital varicella zoster syndrome, fetal varicella zoster syndrome, varicella embryopathy, varicella embryofetopathy, etc. A majority of the cases (90%) of FVS occur as a complication due to maternal varicella infection during the 1 st or 2 nd trimesters of pregnancy, and a few cases (10%) follow maternal herpes zoster [4]. Risk of transmission to fetus is approximately 2% and is especially more common when the mother has infection between the 13 th and 20 th weeks of gestation [3,6]. An excellent review of fetal varicella syndrome (FVS) has been recently published [11]. A recent report [12] has cited the occurrence of the syndrome after maternal varicella at 25 weeks of gestation.

Cicatrical skin lesions with underlying hypoplasia of tissues are well-recognized manifestations . At birth these areas look like area of skin loss that became cicatricial after several weeks. Skin scars are depressed, pigmented and often have a zigzag configuration. Mental retardation, seizures and cortical atrophy may occur. Spinal cord atrophy, limb paresis and cerebellar aplasia have also been reported. Other neurological manifestations include hypotonia, hypereflexia, intermittent myoclonic seizures, dorsal radiculitis, Horner's syndrome, deafness, developmental delay and learning disabilities. Ophthalmological abnormalities include chorioretinitis, nystagmus, anisocoria, microphthalmia, cataract, corneal opacities, squint, hypoplasia of the optic disc and optic atrophy. Skeletal anomalies are limb hypoplasia, equinovarus, calcaneovalgus and hypoplasia of mandible, clavicle, scapula, ribs, fingers and toes. These anomalies arise either directly due to cicatricial lesions causing reduction abnormalities, or could occur secondary to denervation of limbs, which leads to diminished muscle mass and poor growth. Gastrointestinal abnormalities associated with the syndrome include gastroesophageal reflux, duodenal stenosis, jejunal dilatation, microcolon and anal sphincter malfunction. These anomalies probably result due to the damage to the autonomic nervous system and the spinal cord. Neurogenic bladder has been described with FVS .

Varicella infection between 13th and 20th week of pregnancy results into transplacental transfer of the virus re-

sults in fetal viremia and subsequent cutaneous dissemination. The virus then spreads along the cutaneous sensory nerves in a retrograde manner to reach the dorsal root ganglionsatellite cells. Due to the lack of cell mediated immunity before 20 weeks of gestation, the virus remains latent only for a short period of time. Following reactivation, the virus with its neurotropic nature causes further neuronal damage that include necrosis of nerve cells and affection of axons. Considering the pathogenesis some have suggested that it better be referred to as fetal varicella-zoster syndrome [1,10,11]. The criteria for the diagnosis of FVS include maternal varicella during pregnancy, the presence of congenital skin lesions that correspond to dermatomal distribution & immunological evidence of in-utero varicella-zoster infection [13]. This can be proved by demonstration of antivaricella zoster virus IgM in any titer. Maternal samples were considered probable if the IgM was not detected but the IgG titer was 128 or more after 6 months. If suspicious signs are seen on ultrasound, cordocentesis could be used to check for fetal IgM or placental villi could be sampled for VZV DNA detection [8,11]. Definite congenital varicella syndrome means the presence of typical skin scars as well as one of ten additional abnormalities: microcephalus (defined by head circumference less than the 5th percentile for age), ventriculomegaly by ultrasound (defined by a width of either lateral ventricle of more than 10 mm), cerebral cortical atrophy, chorioretinitis, cataract, limb hypoplasia (defined as one limb more than 10% longer than the other), gastrointestinal anomalies or reflux, genitourinary anomalies, sensorineural hearing loss or deficit, or at least one Bayley or Denver neurologic screening delay. Possible cases of congenital varicella syndrome included children with one and only one of the above ten criteria but with no cicatricial skin scarring.

Late onset maternal varicella either may have no effect on the fetus or causes a potentially fatal disseminated infection with widespread cutaneous and visceral affection. The attack rate is estimated to be 24% to 50% and the severity of neonatal disease seems to be dependent on the timing of maternal illness. If mother develops rash five or more days prior to delivery, the infection follows a milder course in her neonate. However, the risk of neonatal death increases if the mother develops rash within four days prior to or upto two days after the delivery [14]. Maternal varicella 5 to 21 days pre-delivery usually results in benign neonatal chickenpox as the baby is protected by transplacentally acquired maternal antibody [15,16]. These neonates develop widespread cutaneous and visceral lesions and develop respiratory distress due to varicella pneumonia. The mortality in such cases could exceed 30%, if left untreated.

Women with definitive history of chickenpox in past could be considered immune but those without such history or with indeterminate history should have their immune status against chickenpox determined. Pregnant women found to be non-immune should receive varicella zoster immune globulin as soon after the exposure as possible [17]. One study has reported that giving VZIG to women who have already developed chickenpox may help prevent fetal infection [18]. Prospective studies will have to be carried out before a general recommendation is made regarding using VZIG in such circumstances. The second issue concerns the use of acyclovir in a pregnant woman. However, its safety in pregnancy has not been extensively studied and is not cleared for use during pregnancy [17].

As started earlier, neonates born to women who develop chickenpox within 5 days before delivery or within two days after delivery are at increased risk for systemic life-threatening disease. These neonates should receive VZIG as soon as possible, so as to attenuate neonatal infection or prevent it totally [18, 19, 20].

Chickenpox is an unusual infection to occur during pregnancy. The risk of FVS following maternal infection is low. However, if VZV infection does occur, it can have disastrous consequences for the pregnant women, fetus and neonate. All pregnant women should be questioned about immunity to varicella during their first antenatal appointment [21]. Those with negative histories could be advised to avoid contact with individuals with chickenpox. Universal immunization using highly immunogenic, effective, and safe vaccine against varicella could prevent varicella infections during pregnancy and in fetus and neonates. However, the cost-benefit ratio of this strategy in developing countries is yet to be evaluated. Termination of pregnancy is not indicated as the risk of fetal damage is less. Plastic surgery may be considered for the scars and limb abnormalities. Our case is being reported to increase awareness about this rare but fascinating condition, which requires a high index of suspicion and careful history for diagnosis.

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