Congenital varicella–zoster virus infection

A rare case of severe brain and ocular malformations without limb or cutaneous involvement in a newborn after maternal subclinical infection

Yousef A. Al-Katawee, *MD,* ***Yousef A. Al-Hasoun,*** *MD,* ***Mohamed N. Taha,*** *MD,* ***Khalid Al-Moslem,*** *MD.*

ABSTRACT

Although congenital varicella-zoster virus (VZV) infection is rare, it carries serious morbidity and mortality to the fetus and newborn infant. We report a full term female newborn infant, born to a multipara unbooked mother who had VZV subclinical infection during the first trimester of pregnancy. Routine newborn examination showed cystic malformation of the left eye, and absence of the right eye globe. Radiological work up revealed severe brain and eye malformations, serological studies of both mother and baby were positive for VZV. The baby underwent palliative surgery to the eyes, upon discharge, a plan of multidisciplinary team was made for follow up including neurologist, ophthalmologist, pediatrician and social worker. Congenital VZV infection can be severe enough to cause catastrophic fetal anomalies and damage to the vital organs as many of those infants die in infancy.

Saudi Med J 2005; Vol. 26 (5): 869-871

Maternal infection with VZV early on during pregnancy (namely, up to 20 weeks gestation) can produce the characteristic malformations of the skin, the brain, the eyes, the extremities, or, rarely, other areas of the body. More over VZV subclinical infection of the pregnant woman can occur after close contact and exposure, which may lead to infection of the fetus. The maternal history, the clinical and the radiological findings as well as the results of laboratory studies were crucial in establishing the diagnosis of varicella-zoster embryopathy. The objectives for reporting this case are to highlight the importance of antenatal follow up and the need for more awareness and attention from the physicians and primary health care personnel towards the pregnant women particularly at first and second trimester of pregnancy to avoid VZV infection to the fetus, and its subsequent serious sequelae to the newborn infant.

Case Report. A 3.15 kg, full-term baby girl was born by spontaneous vaginal delivery, apgar scores were 9 and 10 at the first and fifth minutes to a 42-year-old unbooked grand multipara mother (P7+0). The pregnancy was uneventful, no history

From the Department of Neonatology, Al-Yamamah Hospital, Riyadh, *Kingdom of Saudi Arabia.*

Received 12th December 2004. Accepted for publication in final form 21st February 2005.

Address correspondence and reprint request to: Dr. Yousef A. Al-Katawee, Consultant in Pediatrics & Neonatology, Department of Neonatology Al-Yamamah Hospital, PO Box 106208, Riyadh 11666, *Kingdom of Saudi Arabia.* Tel. +966 (1) 4914444 Ext. 1325/1326. Fax. +966 (1) 4914896 E-mail: yrshmh@hotmail.com

of drugs to mother and there was no history of maternal illness apart from exposure to chicken pox during first trimester where the whole family, including the father, were affected except the mother who was asymptomatic, maternal previous history of chicken pox was uncertain and parents are non-consanguineous. Through routine newborn examination after birth **(Figure 1)**, there was big soft cystic swelling measuring 4 x 5 cm located at the left eye. The right eye was not palpable. Head circumference was 35 cm and length was 49 cm. Other systemic examination including musculoskeletal, extremities and genitalia were normal. Frequent tonic seizures were observed on the 3rd day which was controlled on phenobarbitone.

Initial routine laboratory results as well as ultrasound of abdomen were normal. An MRI of orbits and brain **(Figure 2)** showed huge lobulated soft tissue and cystic density mass lesion occupying the left orbital cavity protruding to the anterior and direct continuation with the left temporal fossa through a widened left inferior orbital fissure. There was bilateral microphthalmia as well as optic atrophy. The brain study revealed a large cyst with hypoplasia of the cerebellum, agenesis of the corpus callosum and single widened central ventricular cavity (holoprosencephaly). Echocardiographic examination was carried out and showed a small secundum atrial septal defect. The infant underwent palliative surgery where the left eye intraorbital cyst was excised and small sized conformer was inserted in the right eye **(Figure 3)**, postoperative findings confirmed the presence of severe bilateral microphthalmia. Histopathological and microscopic examination of the cyst architecture revealed irregular fibro-vascular tissue in some areas and primitive retina-like structures as well as myxoid tissue in other areas, fluid was identified as cerebrospinal fluid. Maternal and infant's serological studies as well as infant's cerebrospinal fluid were positive for varicella-zoster specific IgG antibodies, specific IgM antibodies were negative. The infant's postoperative period was uneventful, and she had a satisfactory general condition upon discharge. At present, she is attending outpatient clinic visits on a regular basis.

Figure 1 - Baby after birth

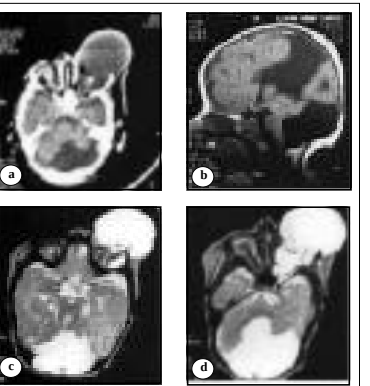

Figure 2 - Orbit and brain imaging studies showing a) axial CT showing posterior fossa and left orbital cyts. b) Sagittal view T1 MRI scan, showing holprosencephaly and cerebellar hypoplasia. c) T2 MRI scan showing bilateral microphthalmia. d) T2 MRI scan showing left orbital cyst in continuation with left temporal fossa.

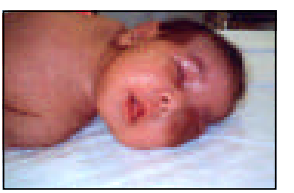

Figure 3 - Baby after palliative surgical repair.

Discussion. Approximately 1-2% are the risks of fetal malformations caused by maternal varicella infection during the first 20 weeks of pregnancy.[1,2] Maternal varicella subclinical infection and congenital varicella syndrome have been reported.[3] The mother in our report was considered to have subclinical infection as there was clear history of exposure to the virus in her first trimester of pregnancy where all members of her family including her husband had chicken pox at this

period. The defects are the result of direct injury of VZV and destruction of the developing fetal tissue in particular that of the nervous system. The range and severity of associated symptoms and physical findings may vary greatly from case to case depending upon when maternal varicella-zoster infection occurred during fetal development. Fetuses infected at 6-12 weeks of gestation appear to have maximal interruption of the limb development where as fetuses infected at 16-20 weeks may have eye and brain involvement,[4] this could explain the limited malformations to brain and eyes only in our case as the mother was exposed to the virus during this period and was confirmed later on by positive varicella specific IgG antibodies. The abnormalities present with congenital varicella syndrome in several large prospective studies include; skin scars, cicatrix (76%), ocular anomalies have been reported as high as (68%),[5] in the form of microphthalmia, optic atrophy, cataract and chorioretinitis; limb or digit hypoplasia (49%) and brain (60%) as aplasia, microcephaly, hydrocephaly.[1,2,6] Isolated brain or eye malformations alone without dermatological involvement have been reported.[7,8] In our case, brain abnormalities were hypoplasia of cerebellum, corpus callosum agenesis and holoprosencephaly,[9-11] the eye abnormalities were bilateral microphthalmia and optic atrophy as well as abnormal retinal structure, these abnormalities together are consistent with the above-mentioned brain and eye abnormalities present with congenital varicella embryopathy, there was no skin or limb involvement.

Diagnosis of the syndrome essentially is clinical: a history of chicken pox to the mother or exposure early on during the first trimester of pregnancy and recognition of the characteristic defects in the neonate.[4,12] The virus cannot be cultured from the affected newborn, and serological studies often have been inconclusive.[4,12] Some infants have VZV specific IgM antibodies detectable in the cord blood sample, although the IgM titre drops quickly postpartum.[4] This could explain why virus specific IgM was negative after birth in the newborn infant. Prenatal diagnosis remains difficult, fetal ultrasound, specific VZV IgM determination in fetal blood and detection of VZV DNA in amniotic fluid or fetal tissue by polymerase chain reaction have been used, but are neither specific nor sensitive for differentiation of congenital varicella syndrome from benign congenital chicken pox.[12] The damage caused by fetal VZV infection does not progress post partum, an indication that there is no persistent viral replication so infants with varicella embryopathy do not require isolation and antiviral treatment is not indicated.[4] Acyclovir treatment may be given to the mother with severe varicella, however neither it's safety nor it's efficacy for the fetus is known.

Acknowledgment. The authors would like to thank Dr. Ahmad Kabbush, Hospital Director and Dr. Fawaz Khalifa, Head of Neonatology Department for their great support.

References

1. Enders G, Miller E, Cradock-Watson J. Consequences of varicella and herpes zoster in pregnancy: Prospective study of 1379 cases, ***Lancet*** 1994; 343: 1547–1560.
2. Pastuszak AL, Levy M, Schick B, Zuber C, Feldkamp M, Gladstone J, et al. Outcome after maternal varicella infection in first 20 weeks of pregnancy. ***N Engl J Med*** 1994; 330: 901-905.
3. Mustonen K, Mustakangas P, Valanne L, Professor MH, Koskinien M. Congenital varicella-zoster virus infection after maternal subclinical infection: clinical and neuropathological findings. ***J Periantal*** 2001; 21: 141-146.
4. Myers MG, Stanberry LR, Seward JF. Varicella-zoster virus. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson Textbook of Pediatrics. 17th ed. Philadelphia, Pennsylvania: WB Saunders; 2004. p. 1059.
5. Andreou A, Basiakos H, Hatzikoumi I, Lazarides A. Fetal varicella syndrome with manifestation limited to the eye: ***Am J Perinatal*** 1995; 12: 347-348.
6. Sauerbrei A, Wutzler P. The congenital varicella syndrome. ***J Perinatal*** 2000; 20: 548-554.
7. Choong CS, Palole S, Whitehall J. Congenital varicella syndrome in the absence of cutaneous lesions. ***J Pediatr Child Health*** 2000; 36: 184-185.
8. Kent A, Paes B. Congenital varicella syndrome: a rare case of central nervous system involvement without dermatological features. ***Am J Perinatal*** 2000; 17: 253-256.
9. Ong CL, Daniel ML. Antenatal diagnosis of a porencephalic cyst in congenital varicella-zoster virus infection. ***Pediatr Radiol*** 1998; 28: 94.
10. Deasy NP, Jarosz JM, Cox TC, Hughes E. Congenital varicella syndrome: Cranial MRI in a long–term survivor. ***Neuroradiology*** 1999; 41: 205-207.
11. Dimova PS, Karparov AA. Congenital varicella syndrome: Case with isolated brain damage. ***J Child Neurol*** 2001; 16: 595-597.
12. Sanchez PJ. Viral Infections of the Fetus and Neonate. In: Feigin RD, Cherry JD, Demmler GJ, Kaplan SL, editors. Textbook of Pediatric Infectious Diseases. 5th ed. Philadelphia, Pennsylvania: WB Saunders; 2004. p. 897-898.