Female Twins with Incontinentia Pigmenti and Concurrent Neonatal Herpes Simplex Virus Infection

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Rows of vesicles over erythematous bases are the typical cutaneous lesions of the first stage of incontinentia pigmenti (IP). But the clinical lesions share the same features with herpetic vesicles. We present a couple of female twins with generalized vesicular eruptions over the trunk and limbs at birth. The pathologic findings were consistent with first stage IP. In addition, an isolated group of vesicles was noted at the vertex of the scalp. Pathologic examination and viral culture proved herpes simplex virus (HSV) infection. Ophthalmologic examination demonstrated retinopathy which consisted of venous engorgement and soft exudates on the retina. Viral cultures of the eyes were positive for herpes virus. Because the course or management of IP and HSV infection is quite different, we suggest that both of the diseases need to be considered in the differential diagnosis of neonatal blistering disorders.


Key words: Incontinentia pigmenti, Herpes simplex virus

第一期色素失禁症的典型皮膚臨床表現是一整排的水泡加上紅色的基底。但是疱疹病毒形成的水泡也會有相同的臨床表現。我們報告一對女性雙胞胎在出生時身體與四肢出現廣泛的水泡分布。病理切片的結果是符合第一期色素失禁症的診斷。除此之外，在她們的頭頂上發現一群獨立的水泡。病理切片與病毒培養證實了其為單純疱疹病毒的感染。眼科的檢查發現有視網膜靜脈擴張與軟性滲出液的視網膜病變。眼睛的病毒培養則長出了疱疹病毒。因爲色素失禁症與單純疱疹病毒感染的病程和處理方式截然不同，我們建議這兩種疾病需要列入新生兒水泡病的鑑別診斷。(中華皮誌21 : 293-297, 2003)
INTRODUCTION

Incontinentia pigmenti (IP) is an X-linked dominantly inherited disease with characteristic skin lesions and stages. Females are mainly affected, and males who got the abnormal gene are usually lethal.1, 2

Linear rows of vesicles over erythematous bases mainly on the extremities and occasionally on the trunk are the typical cutaneous lesions of the first stage of IP. But the clinical lesions share the same features with herpetic vesicles. Because neonatal herpes simplex virus (HSV) infection has the prevalence of 1 in 2000 live births, and it may produce severe complications that complicate the management of infants with IP, we should keep in mind that the possibility of these two diseases may occur in the same patient.3, 4, 5, 6

CASE REPORT

The twins were female newborns born by vaginal delivery to a gravida 4 para 4 (G4P4) mother without abortion history. The mother did not receive any prenatal screens, and she denied any congenital disease or sexual transmitted disease.

Generalized vesicular eruptions over the trunk and limbs of the twins were present at birth. Physical examination revealed that some rice-grain to bean-sized vesicles lying over erythematous bases appeared in a linear distribution on the trunk and limbs (Fig. 1A). The face and neck were not involved. An isolated group of vesicles was noted at the vertex of the scalp since the day of 7 and 8 (twin A and twin B, respectively) (Fig. 2A). Laboratory data showed leukocytosis (WBC: 13200 and 14500,
respectively) and eosinophilia (Eosinophils count: 24% and 25%, respectively). Maternal herpes antibody IgM was positive but IgG was negative. The newborns' herpes antibody IgM and IgG were negative. Pathologic examination of skin biopsy from the vesicles located on the trunk and legs of the twins revealed eosinophilic spongiosis. Individual necrotic keratinocytes were present within the epidermis. Besides, eosinophils also infiltrate in the dermis (Fig. 1B). These pathologic findings were consistent with first stage IP. Pathologic examination of skin biopsy from the vesicles located on the scalp of the twins revealed multinucleated giant cells and balloon cells around the keratinocytes (Fig. 2B). Ophthalmologic examination of the twin B demonstrated retinopathy which consisted of venous engorgement and soft exudates on the retina. Results of bacterial culture from the vesicles located on the scalp, trunk and legs were negative. Tzanck smear from the vesicles located on the trunk, limbs and scalp showed different results. The results of scrapings taken from the trunk and limbs were negative; but from the scalp, we found multinucleated giant cells. Viral culture and monoclonal antibody immunofluorescence proved that there was HSV, type II infection. Viral cultures of the eyes of the twin A were positive for herpes virus. Viral cultures of nasopharynx and cerebrospinal fluid were negative. Except the ocular problems, the twins did not have any other systemic complications such as seizures, encephalitis or skeletal anomalies. Chromosomal studies of the twins showed the normal karyotype 46, XX and no translocation or other chromosome aberration.

Our diagnosis was first stage IP and concurrent neonatal HSV infection. To prevent disseminated HSV infection, they received intravenous and topical acyclovir treatment. When the condition of the female twins became stable, they were discharged and followed up regularly at our hospital.

DISCUSSION

The diagnosis of an inherited cutaneous condition does not exclude the possibility of a coexistence infection and, given the similar clinical presentation of neonatal vesicular eruptions, accurate diagnosis may require skin biopsy and culture. There have been two published articles that reported incontinentia pigmenti and concurrent neonatal herpes simplex virus infection.5, 6

Incontinentia pigmenti (IP) is a rare X-linked dominantly genetic disease with characteristic skin manifestations. This disorder has four stages.7 The first (erythema and vesicular) stage is either present at birth or starts shortly thereafter. It is characterized by linear vesicular eruptions primarily on the extremities and occasionally on the trunk. IP is associated with several abnormalities in the systems such as central nervous system, eyes and teeth.7 Ocular abnormalities occur in about 35% of patients and consist of proliferative vitreoretinopathy, retinal detachment, strabismus, cataract, microphthalmia, and optic nerve atrophy.8 Although our chromosomal studies of the twins showed the normal karyotype and no translocation or other chromosome aberration, we did not exclude the possibility of genetic disorder. Several articles about genetic studies discovered an IP locus at Xq28 which was mapped on the basis of findings from cytogenetic and linkage analysis. Newest genetic studies have demonstrated that mutations in a single gene result in the IP phenotype.9-13

While IP is a rare disease, neonatal herpes simplex virus (HSV) infection may affect 1 in 2000 deliveries. HSV infection of the newborns is usually related to maternal asymptomatic first episode infection in the birth canal during late pregnancy.3 Any area of the skin may be involved, but the grouped vesicles are most commonly present on the scalp or buttock. Monitoring electrodes may produce sufficient skin trauma through which the virus can invade. On rare instance, neonatal HSV lesions may display a linear distribution. Vesicles rarely present at birth. The incubation period of
neonatal herpes is 2 to 21 days and the mean age of onset is 6 days. Eighty percent neonatal infections are HSV-2.3, 4, 14 Neonatal HSV infections are frequently limited to skin, eyes and mucous membranes, but disseminated infection which invades the central nervous system with severe neurodevelopmental sequelae or death can occur.4 The ocular manifestations of herpes infection consist of anterior uveitis and keratitis.15, 16 The majority of these infected newborns present with nonspecific symptoms and signs, such as irritability, lethargy, fever, or failure to feed. Until the disease is far advanced, the diagnosis of neonatal herpes is often ignored. So we should keep in mind that concurrent HSV infection would be in the differential diagnosis of the neonatal blistering diseases because it may complicate the management of infants with IP.5, 6

There have been two published articles about newborns with IP and concurrent neonatal HSV infection.5, 6 In our cases, maternal first episode genital herpes in the late pregnancy led to neonatal HSV infection during labor and delivery. Because maternal HSV seroconversion had not been completed by the time of labor, the newborns did not have the protective antibody against HSV invasion. As mentioned to the ocular complications, the cause of retinopathy was a manifestation of IP-associated anomalies. Although viral cultures of the eyes were positive for herpes virus, no residual neurologic or ocular complications have been detected after preventive intravenous and topical acyclovir treatment. Because the course and management of IP and HSV infection is quite different, we suggest that both of the diseases need to be considered in the differential diagnosis of neonatal blistering disorders.

REFERENCES