Early Congenital Syphilis Presenting with Vesicobullous Eruptions Beyond Palmoplantar Regions

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Despite the fact that congenital syphilis can be easily prevented by detection and treatment of infected expectant mothers, it still occurs with distressing frequency in many parts of the world. Without early diagnosis and adequate antibiotic treatment, it can lead to significant sequelae and even mortality. Clinical manifestations of congenital syphilis are varied, although subclinical cases are more frequent. Bullous eruptions of palmoplantar regions is one of the most characteristic signs (1), although these days it is rarely seen. Additionally, vesicobullous eruptions in congenital syphilis are unlikely to be present in other parts of the body (2). We report a case of a baby who presented with multiple bullae and erythematous macules on the trunk, buttocks, and extremities.

CASE REPORT
A two-month-old female baby presented with erythematous patches with superficial bullae and desquamations on the trunk, buttocks and extremities (Fig. 1). The skin lesions started to appear one month previously and seemed to be spreading. The patient had been born via spontaneous vaginal delivery at 39 weeks' gestation, and she was apparently healthy at birth. The mother was a 22-year-old primigravida who had not received regular prenatal care.

A skin biopsy performed on the buttocks revealed acanthosis, spongiosis and intraepidermal vesicles with neutrophilic infiltrate in the epidermis (Fig. 2A). To exclude the possibility of candidiasis, potassium hydroxide preparation of the vesicle was examined and found to be negative. Blood examination showed leukocytosis (14,870 cells/mm²; normal, 4,000~10,000 cells/mm²), a high erythrocyte sedimentation rate (120 mm/h; normal, 0~20 mm/h) and high level of C-reactive protein (49.0 mg/l; normal, 0~5.3 mg/l). Alanine aminotransferase and aspartate aminotransferase levels were 355 IU/l (normal, 10~40 IU/l) and 201 IU/l (normal, 6~40 IU/l), respectively. A Venereal Disease Research Laboratory (VDRL) test was positive at a titre of 1:32, and Treponema Pallidium Hemagglutination (TPHA) assay was also positive at 1:1280 dilution. Immunohistochemistry using antibodies to T. pallidum (Biocare Medical, Concord, CA, USA) revealed numerous spirochetes in the epidermis (Fig. 2B). On the basis of the data collected, a diagnosis of early congenital syphilis was made. The parents were also positive for both VDRL and TPHA tests. Additional evaluations of the patient were subsequently performed; abdominal sonography was normal without any sign of hepatosplenomegaly. Cerebrospinal fluid analysis showed normal protein and cell counts with a positive VDRL test at a titre of 1:4. Radiography of the long bones showed diffuse bilateral periostitis along the diaphyses of the tibias and metacarpal irregularity at right distal femur, radius and ulna. The patient received 300,000 U/kg aqueous penicillin G intravenously every 8 h for 14 days and her skin lesions resolved completely. Six months after treatment, her VDRL titer was 1:8 and the radiographs of the long bones showed sclerotic metaplasia with clear bony margin suggestive of resolving metaphyseal. Both the parents were treated with Benzathine penicillin G (2.4 million units, IM) weekly for 3 weeks, and the follow-up VDRL titers conducted after 3 months were negative.

DISCUSSION
Congenital syphilis is caused by T. pallidum infection acquired from a mother with untreated or inadequately treated syphilis. Transmission to the foetus can occur during any stage of a pregnancy, and may result in still birth, hydrops fetalis, or preterm birth (3). Approximately 66% of infected infants are asymptomatic at the time of birth (4). Clinical signs can develop weeks, months, or occasionally years later. If manifestations are seen during the first 2 years of life it is considered to be early congenital syphilis, as compared to late congenital syphilis which manifests > 2 years after birth (5).

The most prominent manifestations of early congenital syphilis include fever, rash, hepatosplenomegaly and persistent rhinitis. Lymphadenopathy, neurosyphilis, leukocytosis, thrombocytopenia, and osteochondritis may also be present. The typical skin manifestation is copper-red maculopapular rash most commonly affecting hands and feet. Other cutaneous lesions that may be present include condyloma lata, mucous patches, fissures around the lips or nostrils, and petechiae (6). Case reports of erythema
multiforme-like lesions and pustular lesions have also recently been described (7, 8). A rare bullous variant, known as syphilitic pemphigus, most commonly occurs on palms and soles. Vesicles might be present at birth or occur in the first week of life, and the serous content contain abundant treponemes (2). The vesiculobullous manifestations of syphilitic pemphigus should be differentiated from other bullous and infectious diseases in neonates. Impetigo, candidiasis, hereditary and autoimmune bullous diseases should be included in the differential diagnosis. Initially focussing on the bullous lesions in our patient, we considered chronic bullous disease of childhood as a possible diagnosis, but direct immunofluorescence staining was negative.

The histological features in syphilis include epidermal hyperplasia, spongiosis and basilar vacuolar alteration, often with oedema of the papillary dermis. Exocytosis of lymphocytes, spongiform pustulation, swelling and proliferation of endothelial cells may also be observed. One of the characteristic findings is perivascular and interstitial infiltrates of plasma cells, with variable admixture of lymphocytes and neutrophils. However, there were no plasma cells observed in the biopsy specimen of our patient. When the plasma cell component is inconspicuous or absent in the biopsy specimen, as observed in about 25% of cases (9), diagnosing congenital syphilis can be quite difficult. In our case, the serologic findings of the patient and the mother, along with the immunohistochemical staining result, confirmed the diagnosis of early congenital syphilis.

Our case was notable because while vesicles of syphilitic pemphigus are often limited to palms and soles, our patient had more widespread distribution of the lesions; bullae on the thigh and buttocks, and erythematous macules with desquamation on the hands, flexural part of the arms and legs. She also had crusted patches on the left upper arm, where she previously received a BCG (Bacillus Calmette–Guérin) vaccination, indicating that the lesions had developed in areas that were more vulnerable to trauma.

It is important for clinicians to be aware of the possibility and to always consider congenital syphilis as a differential diagnosis of bullous eruptions in neonates. Screening of all pregnant women with a non-treponemal test at the first antenatal visit and again in late pregnancy (10), especially those who have not had an adequate prenatal care, would also be important to reduce the incidence of congenital syphilis.

The authors declare no conflict of interest.

REFERENCES