
Intravenous Penicillin for Antenatal Syphilotherapy

Henry L. Galan, Paul M. Yandell, and Alfred B. Knight

Department of Obstetrics and Gynecology, Texas A&M University Health Science Center,
Scott and White Clinic and Memorial Hospital, Temple, TX

ABSTRACT

A 21 year old woman (G 2 P0101) of 24 weeks gestation presented with syphilis of unknown duration. Sonography revealed fetal hydrops and placental thickening. Weekly intramuscular injections of 2.4 million U Bicillin for 3 weeks was initiated as recommended by the Centers for Disease Control. Repeat sonogram 1 week after starting treatment revealed increased ascites and a new pericardial effusion. Due to the worsening fetal condition, therapy was altered and the patient was admitted for IV penicillin. She received a continuous infusion of 18 million U penicillin G daily for 10 days. Serial sonograms showed improvement of fetal ascites and pericardial effusion with 10 days of IV therapy, and complete resolution of hydrops was noted within 3 weeks. The fetus was born at term with no stigmata of congenital syphilis on newborn exam, and laboratory tests suggested adequate treatment in utero. © 1993 Wiley-Liss, Inc.

KEY WORDS
Fetal hydrops, congenital syphilis, T. pallidum

In 1987 the incidence of syphilis reached its highest peak since 1950. This increase was greater in women than men, regardless of ethnic group. Furthermore, the increase in congenital syphilis paralleled the rise in women. Benzathine penicillin G is considered the treatment of choice for maternal infection by the Centers for Disease Control (CDC); it prevents neonatal infection in 97–100% of cases. However, if there is reinfection, severe infection, or treatment late in pregnancy (second or third trimester), treatment failure can occur. The CDC has reported that these failures are responsible for 35% of neonatal infections. In the past 20 years, no prospective, randomized study evaluating fetal syphilotherapy has been published.

Left untreated, congenital syphilis has significant perinatal morbidity and mortality, with reported mortality rates of 40–54%. Treatment failure in severe fetal infection may result in fetal death. In a recent case report, Hallak et al. attempted to treat a hydropic fetus with high-dose IV penicillin. They were unable to complete therapy due to fetal distress during fetal blood transfusion that resulted in an emergent cesarean section. We describe a pregnancy with a severely affected fetus that had complete resolution of fetal hydrops and placental thickening 3 weeks after initiation of maternal IV infusion of penicillin G with no clinical stigmata of congenital syphilis identified at birth.

CASE REPORT

A 21 year old black woman (G 2 P0101) at 24 weeks gestation by menstrual and ultrasound dating was diagnosed with syphilis of unknown duration at her initial prenatal visit with the local health department. There was no prior history of syphilis. Her obstetrical history was complicated by prior preterm delivery at 36 weeks gestation in which serology testing for syphilis was negative. She had had multiple sexual contacts in the past. Her rapid plasma reagin (RPR) was 1:64 and microhemag-
glutination assay for antibodies to *Treponema pallidum* (MHATP) was reactive. Spinal tap was not performed because of a normal neurologic examination. She was started on weekly injections of 2.4 million U of Bicillin for 3 weeks as recommended by the CDC for syphilis of unknown duration. An ultrasound performed at the start of therapy revealed fetal hydrops and placental thickening, an enlarged liver, intestinal echodensities, and dilated loops of small bowel. Parvovirus B-19 titers showed immunity. A repeat ultrasound 8 days after initiation of therapy revealed a pericardial effusion and progression of the ascites (Fig. 1).

Due to worsening fetal conditions despite 1 week of Bicillin treatment, the patient was admitted to the antepartum service for aggressive IV penicillin G therapy with doses routinely used to treat adult neurosyphilis. Daily penicillin G at 18 million U continuous IV infusion was initiated and continued for 10 days. The patient tolerated treatment well and remained afebrile throughout her hospitalization. She did not experience the Jarisch-Herxheimer reaction other than a few uterine contractions requiring no tocolysis. No fetal heart rate abnormalities were noted during episodic monitoring.

Serial ultrasound was performed throughout the hospitalization. After 4 days of therapy the ascites and pericardial effusion were unchanged. Six days after therapy there was slight improvement of the ascites. On day 8 of therapy significant improve-
The treatment of both ascites and pericardial effusion were noted. On the day of discharge, following 10 days of IV penicillin, ultrasound revealed even less ascites and the pericardial effusion was just detectable. Three weeks after initiation of treatment, follow-up ultrasound revealed complete resolution of fetal hydrops and placental thickening (Fig. 2). There was good interval growth, and the placenta was no longer hydropic. Ultrasound was performed at 2–4 week intervals until delivery, and all remained normal.

The patient delivered at 37+ weeks gestation after the onset of spontaneous labor. No stigmata of congenital syphilis were evident on the newborn examination. Complete blood count showed no evidence of anemia or thrombocytopenia. Liver function tests were normal. Umbilical cord Venereal Disease Research Laboratory (VDRL) titer was 1:2. Fluorescent treponemal antibody-absorption (FTA-ABS) on serum was 3+ reactive. Cerebral spinal fluid (CSF) VDRL was non-reactive, FTA-ABS was 3+ reactive, and FTA-ABS IgM was negative. CSF gram stain and cultures were negative. The CSF protein was elevated at 194 mg/dl (normal 15–60), glucose was 37 mg/dl (normal 50–80), and the cell count was unremarkable. At the 4 week check, the infant was doing well and had surpassed its birth weight. Repeat VDRL was weakly reactive with 0 dilutions. Repeat CSF studies showed an improved, yet persistantly elevated protein of 123 mg/dl. At the 2 month check, the infant was progressing well and was neurologically intact. VDRL was nonreactive and FTA-ABS was 3+ reactive. It was felt that the infant had been treated adequately in utero and that the decreasing levels of CSF protein represented a normalizing trend. However, because the consequences of early childhood neurosyphilis are tragic and there was concern about the ability to follow this child closely over a longer period of time, the infectious disease consult service chose to treat the child again with 200,000 U of aqueous penicillin G IM twice daily for 14 days.

**DISCUSSION**

With the decline in incidence of Rh isoimmunization, fetal hydrops is more commonly of infectious origin. A review of the literature by Hallak et al. revealed only 14 cases of nonimmune hydrops due to syphilis. Other infectious etiologies of nonimmune hydrops cited were cytomegalovirus, bacteria, toxoplasmosis, rubella, herpes, *Listeria*, and *Chlamydia*. Although fetal hydrops due to syphilis is rare, it is likely to increase along with the increasing incidence of congenital syphilis.

The current CDC recommended treatment for syphilis in the pregnant individual is similar to that of the nonpregnant individual. The literature reflects uncertainty regarding the efficacy of this treatment, as shown by the number of studies reporting treatment failures, which account for 3.5% of neonatal infections. A well-controlled evaluation of the current CDC-recommended treatment for syphilis in pregnancy has not been reported, in part because of our inability to measure the response of the disease to therapy.
However, sonography is a mechanism by which the response to therapy of the severely infected fetus can be monitored.

In a 1988 publication, Wendel notes that women treated in the late second or third trimester of pregnancy may deliver affected infants prematurely or experience fetal demise soon after therapy, the latter possibly occurring secondary to the Jarisch-Herxheimer reaction. He also states that benzathine penicillin may prevent congenital syphilis, but that it may not alter the course of severe fetal disease. Several reports have documented high perinatal mortality with fetal hydrops due to syphilis. Therefore, doses that are normally used to treat adult neurosyphilis may attain serum and amniotic fluid levels high enough to treat severe infections in utero.

The rapid response to high-dose penicillin G therapy and lack of syphilis stigmata at birth suggest that this means of treatment may serve a role in the severely affected fetus, particularly late in pregnancy. The availability of high-resolution sonography provides a means to closely monitor the response of the disease to treatment closely. Further investigation is warranted to evaluate the efficacy of high-dose IV penicillin versus current CDC recommended treatments for the severely syphilitic fetus.

REFERENCES

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