1987

Reprinted from NEW YORK STATE JOURNAL OF MEDICINE, Vol. 87, November 1987.
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Stillbirth following maternal Lyme disease

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Borrelia infection acquired during gestation may result in death or malformation of the developing fetus.[1-3] This report describes a clinicopathologic investigation of a stillborn fetus that led to a retrospective diagnosis of Lyme disease contracted during the first trimester of pregnancy.

CASE REPORT

A 24-year-old woman enjoyed frequent hikes in the Wasatch mountains outside of Salt Lake City, Utah, in the spring and summer of 1984. In mid-July she was told by her physician that she was approximately eight to ten weeks pregnant. She moved to Southampton, New York, in September 1984. Regular prenatal care was supervised by an obstetrician. Her antepartum course was uneventful until February 9, 1985, when spontaneous labor commenced on the expected day of confinement. Fetal heart sounds were undetectable when she arrived at the hospital, and an ultrasound examination confirmed fetal demise. A 2,500-g stillborn was delivered vaginally. An autopsy of the fetus was requested.

Following completion of the autopsy, the pathologist and obstetrician interviewed the patient for any previous history of signs and symptoms associated with Lyme disease. She reported that following a hike in one of the parks in Wasatch County in May 1984, a red-purple lesion of the skin had developed near the left knee. She presumed that she had been bitten by a small insect. The lesion enlarged to become an annular erythematous patch approximately 14 cm in diameter and then gradually faded and disappeared. Several days after the onset of the skin lesion, pain and swelling developed in the left knee, lasting approximately one week. She did not seek medical attention for these symptoms. With the exception of oral digoxin, 0.5 mg daily, prescribed for mitral valve prolapse, she had taken no medications while pregnant.

A standard autopsy was performed, supplemented by cultures of fetal liver, spleen, kidney, and heart in Barbour Stoenner Kelly medium,[4] which supports the in vitro growth of *Borrelia* spirochetes. Paraffin sections of formalin-fixed autopsy tissues were examined by indirect immunofluorescence (IFA)[5,6] and Warthin Starry silver impregnation. Maternal serum obtained ten days following delivery was divided into three aliquots, and Lyme serologic tests were performed at the Centers for Disease Control (Atlanta, Ga), New York State Department of Health, and Yale University (New Haven, Conn) by IFA and enzyme-linked immunosorbent assay (ELISA) methods.[7,8] *Treponema pallidum* serologic tests were done by the Treponema Research Branch at the Centers for Disease Control.

The fetus showed early cutaneous maceration and no external malformations. Radiographs disclosed no skeletal anomalies. A 4-mm defect in the muscular portion of the basal interventricular septum was classified as an atrioventricular canal ventricular septal defect by a consultant in cardiac pathology (Jesse E. Edwards, MD). No other malformations were identified. The placenta weighed 270 g; the disc measured 17 × 12 × 2 cm; and serial sections revealed no gross abnormalities in the cotyledons, or infarctions, intervillous thrombi, or evidence of abruption.

Spirochetes were recovered from fetal liver, but primary cultures and subcultures were contaminated with bacillus species. The cultured spirochetes bound the mouse IgG monoclonal antibody H5332 (provided by Dr Alan Barbour, Rocky Mountain Laboratory, Hamilton, Mont). Antibody H5332 recognizes the outer surface membrane of *Borrelia burgdorferi*.

Routine sections of fetal tissues showed mild autolysis and no significant inflammation. Placental tissues showed rare plasma cells in isolated villi. Spirochetes were identified by immunofluorescence in the fetal myocardium, adrenal gland, and subarachnoid space of the midbrain; and silver stains disclosed rare spirochetes in the myocardium, placenta, liver, and brain.

Lyme serologic studies on postpartum maternal blood were positive at two of three laboratories by IFA methods and by ELISA methods, but negative by IFA and ELISA at a third laboratory. Serologic tests for syphilis, including the RPR, MHA-TP, and FTA-ABS, were negative at the Centers for Disease Control.

DISCUSSION

Transmission of the spirochete *Borrelia burgdorferi* from mother to fetus during the first trimester of pregnancy was followed by overwhelming spirochetosis in the fetus, with intrauterine death near term. Maternal infection was acquired in the state of Utah, where the tick *Ixodes pacificus* is known to be a vector of *B burgdorferi*.[9,10]

The observations in this case complement those of Schlesinger et al,[11] who described the first case of maternal-fetal transmission of *B burgdorferi* in a young pregnant woman who acquired Lyme disease while camping in Wisconsin. Her infant died 39 hours after birth of complications related to a complex congenital cardiac malformation. Although spirochetes were not found in the myocardium, rare spirochetes were seen in fetal kidney, spleen, and bone marrow. No attempt was made to culture spirochetes from autopsy tissues. Maternal serum was reactive against *B burgdorferi* by IFA and ELISA methods at two laboratories and was falsely nonreactive at a third laboratory.

Symptoms of Lyme disease are protean, and although the characteristic expanding annular erythema followed by arthritis was present in this case, many other clinical presentations are possible in cases in which cutaneous or articular symptoms are absent.[12,13] And, as we describe in this report, even classical symptoms may be overlooked by the patient and her physicians unless

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a specific set of questions is included in the patient's review of symptoms. The clinical examination of the patient and the clinical diagnosis of probable Lyme disease must be the "gold standard of diagnosis," because Lyme serologic studies may be nondiagnostic due to interlaboratory variation in detection of serum antibody[14] or due to the delay between primary infection and the production of serum antibody, which is recognized for every serologically defined infectious disease.

Two cases of transplacental transmission of *Borrelia burgdorferi* have been associated with fetal death and cardiac malformation. Different anomalies were found in each case; therefore, a cause and effect relationship cannot be determined between the spirochete in tissue and a specific lesion. We recommend that pathologists search for spirochetes in tissues of stillborn fetuses who show malformations in the cardiovascular system. Clinicians should investigate the possibility of exposure to Lyme disease during the first trimester of pregnancy in such cases, for cardiac organogenesis is essentially complete at the end of the first trimester of gestation.[15]

We believe that evidence is now sufficient to specifically alert women who live in endemic areas for Lyme disease and their physicians to recognize the signs and symptoms of infection by *Borrelia burgdorferi* and related *Borrelia* species. It is our further recommendation that pregnant women with symptoms of Lyme disease be treated immediately with penicillin in doses equivalent to those used for syphilis in pregnancy, and that therapy not be delayed or withheld pending results of serologic studies.

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