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NEWSLETTER

Bartonella and Pregnancy[©]

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In This Issue:

Once again I (Dr. Hardy) am writing a Newsletter after a major natural disaster. Hurricane Sandy just passed violently through the northeast and hit New Jersey very hard. I am writing this Newsletter on the 6th powerless day on a laptop computer by the light of a battery operated lantern. Be that as it may, the fall 2012 issue of the NVL Newsletter will review *Bartonella* and reproduction and pregnancy.

Bartonella and Reproduction:

We will consider *Bartonella* interaction with reproduction: conception, transplacental (vertical) transmission, pregnancy, health of the fetus and neonate, and finally the long term health of the offspring. As has been discussed in previous Newsletters, *Bartonella* are bacteria that can induce silent infections or inflammation in infected animals. The inflammation often is subtle and chronic and may be difficult to identify an infected animal as having a "disease." *Bartonella* infect erythrocytes, leukocytes and especially endothelial cells that line the entire circulatory system. They carry proteins that induce cytokine production which can initiate inflammation. Inflammation of the reproductive organs may lead to reproductive disorders of poor conception, failure to carry to term, infected fetuses that may be unthrifty, and even cause spontaneous abortions. A review of the literature shows a dearth of publications regarding *Bartonella* effects on reproduction.

The pet cat, the major reservoir for the *Bartonella* species that infect people, appears to be a vigorous fertile species despite the fact that about 38% of healthy cats in this country are chronic carriers of the bacteria.¹ In this regard, humans are the most common accidental recipient for feline *Bartonella* and there is little in the literature regarding the possible reproductive complications of this zoonosis.

Conception- Reproductive Difficulties:

Evidence of reproductive difficulty or failure to conceive was observed in all 5 *Bartonella* experimentally infected cats but not in the one control uninfected cat.²



Three of the infected cats required repeated breedings in order to conceive, whereas the control conceived after only 1 breeding. The remaining 2 infected cats never conceived or failed to maintain their pregnancies. The authors did not find evidence of transplacental, colostral, perinatal, or venereal transmission. However, aborted fetuses of naturally infected pet cats have not been examined for the presence of *Bartonella*.

Transplacental Transmission:

Transplacental (vertical) transmission of *Bartonella* has been shown to occur in animals and is a concern for veterinarians and physicians. Transplacental transmission occurs in mice, cattle, and horses infected with *Bartonella birtlesii*, *Bartonella bovis* and *Bartonella henselae*.³⁻⁶

Rodents:

An early study of naturally infected cotton rats and white-footed mice found that all of the embryos from infected mothers were also infected with *Bartonella*. This shows that vertical transmission of *Bartonella* occurs routinely in wild rodents.³

Significant reproductive disease was demonstrated in an experimental study of 20 mice, infected before conception, with *Bartonella birtlesii*, a rodent derived *Bartonella* species.⁴ Fetal death and resorption was 36.3% in infected mice versus 14.5% for controls. Weight of viable fetuses was considerably lower than for uninfected controls.



76% of the fetal resorptions were culture positive for *B. birtlesii* demonstrating transplacental transmission. The placentas of infected mice histologically had typical *Bartonella* vascular lesions in the maternal placenta. This study showed that *Bartonella* is capable of significantly affecting pregnancy and the health of the fetus.

Cattle:

A study of a closed 448 cow dairy herd in France found there was a 59% prevalence of *Bartonella* infection (bacteremia) which increased with age to 90% in animals 1-2 years old.⁵ The level of bacteremia (CFU per ml blood) was highest in



pregnant animals. Abortion and embryonic death were increased in infected animals, marginally significant ($P=0.06$), but there was no decrease in breeding efficiency or interval between 2 calvings.

Horses:

A near-term spontaneous aborted quarter horse fetus was obtained from a mare with no clinical sign of illness and no history of prior abortions,⁶



The usual agents of equine abortion were all absent. The fetus had multiple tan 1-3 mm diameter foci scattered throughout the liver, kidneys, lungs and adrenal glands. Histologically the foci had areas of inflammation, necrosis and vasculitis, typical lesions seen in humans, cats and dogs infected with *Bartonella*. Colonies of Gram-negative, Warthin-Starry silver stain positive bacteria were present in the lesions and nucleotide sequences were 99.9% homologous with *B. henselae*. It is apparent that *B. henselae* caused the death of this equine fetus.

Pregnancy- Humans:



Pregnancy and Bartonella
Photo credit: Shutterstock.com

Molecular evidence of perinatal transmission of *Bartonella vinsonii* subsp. *berkhoffi* and *Bartonella henselae* to a child. Breitschwerdt, EB, Maggi, RG, Farmer, P, and Mascarelli, PE. J Clin Microbiol. 48:2289-2293, 2010.

This is a disturbing report of apparent perinatal transmission of 2 *Bartonella* species, *Bartonella vinsonii* subsp. *berkhoffi* and *Bartonella henselae*, in twins of an infected mother and father.⁷ The parents had extensive cat exposure and persistent symptoms common to *Bartonella* infection including: frequent headaches, memory loss, insomnia, confusion, irritability, arthralgia and myalgia, and the inability to conceive. They

eventually conceived twins by *in vitro* fertilization and delivered them by cesarean section. The twin sister died at 9 days due to hypoplastic left heart syndrome. The parents had received multiple long term antibiotic therapy with doxycycline, azithromycin and ciprofloxacin without any symptomatic improvement. The surviving son had multiple symptoms similar to his parents. *Bartonella* species were identified in the paraffin-embedded tissues of the female twin, and cervical and placental biopsy tissues from the mother and from the blood of the father. The availability of paraffin tissue from a previous uterine biopsy enabled confirmation of infection of the mother with *Bartonella henselae* 10 years before *in utero* or perinatal transmission to her children. The authors concluded that it is plausible that the twins were infected *in utero*, after which the son maintained a persistent infection for 10 years.

Cat Scratch Disease During Pregnancy. Bilavsky, E., Amit, S., Avidor, B., Ephros, M, and Giladi, M. *Obstet. Gynecol.* 119: 640-644, 2012.

There are very few reports of *Bartonella* infection during pregnancy in humans. This group from Israel described the clinical manifestations of CSD occurring in 8 pregnant women over a 19 year period during which there were 1,630,709 total births in Israel.⁸ They reported on the pregnancy outcomes and long term follow-ups of these children. This is an important study since many veterinarians are concerned about the obstetrical public health implications to women and their fetuses of *Bartonella* infections during pregnancy.

Study Data:

Patients 1 through 8:

1. 29 yr-old with typical CSD, 8 wks pregnant
2. 34 yr-old with typical CSD, 16 wks pregnant
3. 28 yr-old with typical CSD, 4 wks before conception
4. 29 yr-old with typical CSD, 4-8 wks pregnant
5. 25 yr-old with typical CSD, 22 wks pregnant
6. 33 yr-old with atypical CSD*32 wks pregnant
7. 37 yr-old with typical CSD, 5 wks pregnant
8. 37 yr-old with typical CSD, 10 wks pregnant

*Neuroretinitis in right eye, no lymphadenopathy

History of cat contact for each patient:

1. Extensive cat & kitten exposure
2. Occupational exposure to cats & other animals
3. Cat scratch 1 month before
4. Kitten bite 1 month before
5. Indirect contact with sandbox used by cats
6. Cat owners who often fed stray cats
7. Cat owner- direct contact
8. Cat owner- often scratched by stray cats

Laboratory diagnosis for each patient:

1. Serology: IgM seroconversion
2. Serology: IgM & IgG seroconversion
3. Serology: IgG, PCR: *B. henselae* DNA
4. Serology: IgM & IgG
5. Serology: IgG
6. Serology: IgM & IgG
7. Serology: IgG
8. Serology: IgG, PCR: *B. henselae* DNA

Treatment* and response during pregnancy:

1. Penicillin V followed by cephalexin- no response mentioned
2. No therapy mentioned
3. Clindamycin- no improvement
4. No therapy mentioned- terminated pregnancy
5. Several courses of antibiotics (not identified)- lymphadenopathy worsened
6. No therapy mentioned
7. Oral antibiotics (not identified)- improved
8. No treatment due to spontaneous abortion

* Azithromycin is often prescribed for CSD and is considered safe in pregnancy; however doxycycline is often prescribed for atypical CSD and is contraindicated during pregnancy.

Pregnancy outcome and neonatal follow-up:

1. Normal delivery & normal- 5.5 yr follow-up
2. Normal delivery & normal- 6 mos follow-up
3. Normal delivery & normal- 7 mos follow-up
4. Termination of pregnancy**
5. Normal delivery & normal- 3.5 yr follow-up
6. Normal delivery & normal- 1y 10m follow-up
7. Normal delivery & normal- 9.5 yr follow-up
8. Spontaneous abortion⁺

** Patient #4 developed a painful axillary lymphadenitis 1 month after the bite from a kitten, and had a chest and abdominal CT scan due to a fear of possible cancer because of an extensive history of breast cancer in the patient's family. Eight weeks after the beginning of her illness serum antibody to *B. henselae* IgM and IgG were detected. At that time the patient learned of her pregnancy and, due to the exposure of the CT high-dose radiation during her early pregnancy, this patient elected to terminate her pregnancy. This case demonstrates the problem that may transpire due to physician's lack of awareness of CSD. Despite the classic sign of CSD in this young patient, painful lymphadenopathy occurring several weeks after a kitten bite on the ipsilateral upper arm, malignancy rather than CSD was considered and investigated by abdominal CT before pursuing serologic diagnostic tests for CSD. The patient subsequently decided to terminate her pregnancy over concerns of high dose radiation to her fetus despite the medical guidelines that indicate diagnostic CT would not deliver sufficient radiation to justify pregnancy termination.⁹

⁺ Patient 8 had a spontaneous abortion at week 10 of her pregnancy, just 7 weeks after the clinical onset of CSD. Unfortunately, there was no pathological examination of the aborted fetus or the placenta.

There was no evidence of transplacental transmission of *B. henselae* in patient #2 who had amniocentesis which was PCR-negative for *Bartonella*. The conclusion of this study in the author's words: "With the exception of one early spontaneous abortion, in which causality to cat scratch disease could not be established, neither deleterious effects of cat scratch disease on newborns nor reports of long-term sequelae were found." In another interpretation, Dr. Todd Florin, a senior fellow in pediatric emergency medicine at the Children's Hospital of Philadelphia, who was not involved in this study, said "I think we can find some mild amounts of

reassurance by saying, 'well, six out of these eight pregnancies ended in a normal, healthy live birth.'"

Bartonella Tests of Cats from Pregnant Owners:

We found 78 of 217 (36%) cats living in households with a pregnant owner to be serologically positive by western blot. None of the test submissions indicated any difficulty with the pregnancy of the owners.

Summary:

These reports show that transmission of *Bartonella* can occur during pregnancy in animals and apparently rarely in humans. The placental anatomy is very variable among mammals and we must interpret the animal studies with caution as some animal placentas may permit vertical transmission more readily than others. We feel that veterinarians should take the lead in educating the public on the general dangers of feline *Bartonella* zoonoses and warn pregnant owners to avoid contact with *Bartonella*-infected cats until they have been treated. In addition, obstetricians and gynecologists must become more familiar with *Bartonella* symptoms in their patients.

We would like to hear from female veterinarians or female veterinary technicians who were diagnosed with CSD or *Bartonella* infection, or thought they might have been infected, before or during their pregnancy.

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