Title

Complex cutaneous leishmaniasis in pregnancy.

Authors

Zachek, Christine M
Osuoji, Olive
Qendro, Isabella
et al.

Publication Date

2023-03-01

DOI

10.1016/j.ajog.2023.02.027

Peer reviewed

Complex cutaneous leishmaniasis in pregnancy

Christine M. Zachek, M.D. M.P.H., Olive Osuoji, M.D., Isabela Qendro, M.D., Omonigho Aisagbonhi, M.D. Ph.D., Richard Wolf, D.O. M.P.H., Brian Hinds, M.D., Scott A. Harvey, M.D. M.S.

PII: S0002-9378(23)00141-2

DOI: https://doi.org/10.1016/j.ajog.2023.02.027

Reference: YMOB 14980

To appear in: *American Journal of Obstetrics and Gynecology*

Received Date: 23 January 2023

Accepted Date: 28 February 2023

Please cite this article as: Zachek CM, Osuoji O, Qendro I, Aisagbonhi O, Wolf R, Hinds B, Harvey SA, Complex cutaneous leishmaniasis in pregnancy, *American Journal of Obstetrics and Gynecology* (2023), doi: https://doi.org/10.1016/j.ajog.2023.02.027.

Title: Complex cutaneous leishmaniasis in pregnancy

Authors:

Christine M. ZACHEK M.D. M.P.H.[1], Olive OSUOJI M.D.[2], Isabela QENDRO M.D.[1], Omonigho AISAGBONHI M.D. Ph.D.[3], Richard WOLF D.O. M.P.H.[1], Brian HINDS M.D.[2], Scott A. HARVEY M.D. M.S.[1]

[1] Department of Obstetrics, Gynecology and Reproductive Sciences, University of California San Diego, San Diego, CA.

[2] Department of Dermatology, University of California San Diego School of Medicine, San Diego, CA

[3] Department of Pathology, University of California San Diego, San Diego, CA.

Corresponding Author:

Christine Zachek, MD MPH

University of California San Diego

Department of Obstetrics, Gynecology & Reproductive Sciences

9300 Campus Point Drive, MC 7433, La Jolla, CA 92037-7433

Phone: 858-249-1206, Fax: 858-657-7212

Email: cmzachek@health.ucsd.edu

Word Count: 721

Conflicts of Interest: The authors have no conflicts of interest.

Funding: The authors have no funding sources to disclose.

Tweetable Statement: Cutaneous leishmaniasis can present more aggressively during pregnancy resulting from relative immunosuppression. Documenting a travel history and maintaining a high index of suspicion for tropical diseases are important when caring for refugee populations.

Short Title: Cutaneous leishmaniasis in pregnancy

Key Words: pregnancy dermatoses, leishmaniasis, tropical diseases, fetal growth restriction, preterm birth, maternal floor infarction

A previously healthy 30-year-old G4P3004 Haitian refugee presented to prenatal care at 31 weeks of gestation with a four-week history of large crusted and ulcerated plaques on her lower extremities and face. She recently sought refugee status in the United States following land migration through Central and South America, where she intermittently slept in the wilderness and near bodies of water. On initial examination in the emergency department, she was afebrile. Skin examination revealed 2-6 cm tender, crusted plaques on the left cheek (Figure 1), right lateral knee (Figure 2) and left medial thigh with peripheral hyperkeratosis, satellite papules, and central ulceration with purulent drainage. There was no mucosal involvement. Laboratory studies showed no abnormalities on complete blood count, chemistries, or liver function tests. She was discharged on oral clindamycin and topical mupirocin.

She re-presented 3 weeks later with interval development of a new skin lesion and was admitted for expedited work-up and wound care. Routine prenatal labs including HIV, syphilis, hepatitis, QuantiFERON, chlamydia and gonorrhea were negative. Dermatology and infectious diseases were consulted with suspicion for leishmaniasis based on the lesion morphology and travel history. Skin biopsy was sent for pathology, tissue culture, and PCR testing. Obstetric ultrasound was notable for an enlarged placenta, normal amniotic fluid index, and growth restricted fetus, and a course of betamethasone was administered for fetal lung maturity. Maternal abdominal ultrasound was unremarkable for visceral involvement.

While awaiting diagnostic studies, the patient was presumptively treated for leishmaniasis with liposomal amphotericin B (3 mg/kg/day) for 7 days. Daily renal, liver function, and electrolytes

were monitored. A repeat ultrasound showed symmetric fetal growth restriction (<1%) with mildly resistive umbilical artery Doppler studies and thickened, 7.5cm heterogeneous placenta.

Skin biopsy showed pseudoepitheliomatous hyperplasia with neutrophilic microabcesses, plasma cells, and small intracytoplasmic organisms on Giemsa staining (Figure 3), consistent with leishmaniasis. PCR testing later confirmed *Leishmaniasis panamensis* speciation. Stool ova and parasite cultures were positive for *Giardia lamblia* and metronidazole was initiated. Comprehensive work-up for viral, bacterial, and fungal pathogens was otherwise negative.

During hospitalization the patient developed preeclampsia without severe features. At 35 weeks and 6 days, fetal heart rate monitoring became non-reassuring and the decision was made to proceed with cesarean delivery. A viable female infant was born weighing 1815g. Placental pathology showed massive perivillous fibrin deposition (maternal floor infarction) covering 70% of the placental disk sampled without evidence of leishmania infection (Figure 4).

On outpatient follow-up the patient had minimal clinical response to amphotericin B and transitioned to fluconazole therapy 600mg daily. Her skin lesions were resolving, with decreased pain and no new lesions after three months of continuous therapy (Figure 5).

Cutaneous leishmaniasis is characterized by an exaggerated immune response to parasitic infection, causing ulcerative lesions and lymphadenopathy.[1] Physiologic changes of pregnancy cause relative immunosuppression, and the imbalance of Th-1 and Th-2 type immunologic response can increase susceptibility to leishmaniasis and cause a more pronounced disease

phenotype.[2] Studies have demonstrated that infected pregnant persons develop larger lesions with distinct macroscopic findings, and case-control studies have suggested an increase in preterm delivery and stillbirth.[3] Whether leishmaniasis was contributory to our patient's outcome is unknown; this calls for further research. The massive fibrin deposition noted on placental pathology is associated with maternal autoimmune conditions and likely contributed to the observed fetal growth restriction.[4]

Treatment of leishmaniasis during pregnancy is complicated by teratogenicity of first-line medications. However, the literature supports the use of amphotericin B, particularly in cases of visceral leishmaniasis[2] and in cases of atypical disease, mucosal involvement, or disfiguring facial lesions, such as in our patient. Healing of cutaneous leishmaniasis continues after the treatment course is completed and is assessed clinically by the physical appearance of lesions, as shown in our patient.

Global elimination of visceral and cutaneous leishmaniasis has remained elusive – displacement resulting from conflicts in endemic areas have resulted in continued transmission.[5] As our case illustrates, altered migration patterns related to climate change and globalization, among other sociocultural conflicts have contributed to newer distributions of neglected tropical diseases. This is the first case report, to our knowledge, of cutaneous leishmaniasis during pregnancy diagnosed in the United States. Our case illustrates the importance of a thorough travel history and maintaining a high index of suspicion for tropical diseases when caring for refugee populations. Early multidisciplinary collaboration should be considered for complex infectious disease diagnosis and care coordination in marginalized groups.

Acknowledgements: We would like to thank the patient for allowing the use of her images to advance clinical knowledge. In addition, we would like to acknowledge the team of providers including perinatologists, neonatologists, pathologists, dermatologists, infectious disease specialists, and social workers involved in this patient's care.

References:

1) Dutra WO, Barbosa DF, de Souza PEA, Morgan D, Poetker S, Guimarães LH, Bacelar O, Gollob KJ, Carvalho EM. A Th2-Type Response Is Associated With Exuberant Lesions in Pregnant Women Infected With Leishmania braziliensis. J Infect Dis. 2019 Jan 9;219(3):480-488. doi: 10.1093/infdis/jiy510. PMID: 30165577.

2) Conceição-Silva F, Morgado FN, Pimentel MI, e Vasconcellos Ede C, Schubach AO, Valete-Rosalino CM, Kropf P, Müller I. Two women presenting worsening cutaneous ulcers during pregnancy: diagnosis, immune response, and follow-up. PLoS Negl Trop Dis. 2013 Dec 12;7(12):e2472. doi: 10.1371/journal.pntd.0002472. PMID: 24349585; PMCID: PMC3861112.

3) Morgan DJ, Guimaraes LH, Machado PR, D'Oliveira A Jr, Almeida RP, Lago EL, Faria DR, Tafuri WL, Dutra WO, Carvalho EM. Cutaneous leishmaniasis during pregnancy: exuberant lesions and potential fetal complications. Clin Infect Dis. 2007 Aug 15;45(4):478-82. doi: 10.1086/520017. Epub 2007 Jul 5. PMID: 17638198.

4) Devisme L, Chauvière C, Franquet-Ansart H, Chudzinski A, Stichelbout M, Houfflin-Debarge V, Subtil D. Perinatal outcome of placental massive perivillous fibrin deposition: a case-control study. Prenat Diagn. 2017 Apr;37(4):323-328. doi: 10.1002/pd.5013. Epub 2017 Mar 24. PMID: 28152557.

5) Burza S, Croft SL, Boelaert M. Leishmaniasis. Lancet. 2018 Sep 15;392(10151):951-970. doi: 10.1016/S0140-6736(18)31204-2. Epub 2018 Aug 17. PMID: 30126638.

Figure Legends:

Figure 1. Facial cutaneous leishmaniasis lesions

Figure 2. Right knee cutaneous leishmaniasis lesions

Figure 3. Cutaneous leishmaniasis lesions, hematoxylin and eosin stain (magnification 200X) – arrows represent macrophages containing numerous intracytoplasmic kinetoplasts

Figure 4. Placental pathology with massive perivillous fibrin deposition, hematoxylin and eosin stain (magnification 100X)

Figure 5: Healing right knee lesion two months after initial presentation