ELSEVIER

Contraception 81 (2010) 150–156

Contraception

Original research article

Early molar pregnancy: experience in a large abortion service☆

Maureen Paul[a,b,*], Suzan Goodman[c], Juan Felix[d,e], Rebekah Lewis[f], Mitchel Hawkins[g], Eleanor Drey[g]

[a]Planned Parenthood of New York City, New York, NY 10012, USA
[b]Department of Obstetrics, Gynecology and Reproductive Science, Mt. Sinai School of Medicine, New York, NY 10029, USA
[c]Department of Family and Community Medicine, University of California, San Francisco, San Francisco, CA 94110, USA
[d]Department of Pathology, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA
[e]Department of Obstetrics and Gynecology, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA
[f]Department of Sociology, McGill University, Montreal, Quebec H3A 2T7, Canada
[g]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, CA 94110, USA

Received 10 March 2009; revised 12 August 2009; accepted 20 August 2009

Abstract

Background: With 1.1 million US women having first-trimester abortions annually, clinicians have an opportunity to diagnose molar pregnancy early. Early moles, however, may lack "classic" diagnostic hallmarks.
Study Design: This study aimed to assess the accuracy of the diagnosis of hydatidiform mole in women seeking abortion services at a large Planned Parenthood affiliate. We retrospectively identified women with a histopathologic diagnosis of mole from the affiliate's risk management database. The tissue specimens were reviewed by an expert independent pathologist and analyzed by flow cytometry and $p57^{KIP2}$ immunohistochemical staining to clarify the diagnosis.
Results: Of 21 patients who received an initial histopathologic diagnosis of mole, only six proved to have the condition. The interobserver correlation coefficient (kappa) for pathology examination was (−) 0.353. Overdiagnosis of partial moles was the most common error.
Conclusions: Improved, cost-effective strategies for detection of early moles would benefit patients and providers.

Keywords: Hydatidiform mole; Molar pregnancy; Early hydatidiform mole; Gestational trophoblastic disease

1. Introduction

Hydatidiform mole occurs in about one in 1000 pregnancies in the United States [1]. Approximately 15% of patients with complete moles and 0.5% of those with partial moles will develop persistent gestational trophoblastic neoplasia (GTN) requiring postevacuation chemotherapy [2,3]. Most cases of persistent GTN occur within 6 months of evacuation [4], and serum quantitative human chorionic gonadotropin (hCG) surveillance remains the chief means of detection. The American College of Obstetricians and Gynecologists (ACOG) currently recommends obtaining a baseline serum hCG level within 2 days of evacuation of a molar pregnancy, if possible, repeating the test every 1–2 weeks until negative and then testing monthly for another 6 months [4]. Rising or plateauing hCG concentrations in the absence of a new pregnancy signify persistent GTN.

Each year in the United States, nearly 1.1 million women obtain abortion services during the first trimester [5,6], providing a unique opportunity for clinicians to diagnose molar pregnancies early. Early diagnosis presents challenges, however, because patients may lack "classic" molar hallmarks, such as anemia, excessive uterine enlargement or the typical "snowstorm" pattern on sonogram [7–12]. Moreover, the distinctive histopathologic changes of "classic" hydatidiform moles may be subtle or absent in early moles [13,14].

The aberrant fertilization that gives rise to hydatidiform moles forms the basis for adjunctive tests that may assist in the diagnosis [12,15]. Partial moles are typically triploid with

☆ Disclaimer: The opinions expressed in this article do not necessarily reflect those of Planned Parenthood Federation of America, Inc.

* Corresponding author. Planned Parenthood of New York City, New York, NY 10012, USA.
E-mail address: maureen.paul@ppnyc.org (M. Paul).

0010-7824/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.contraception.2009.08.007

one maternal and two paternal haploid sets of chromosomes [16]. Complete moles usually have a diploid karyotype derived exclusively from the paternal genome, although tetraploid and aneuploid complete moles occasionally have been reported [17,18]. Immunohistochemical staining with antibody to $p57^{KIP2}$, a protein that is paternally imprinted yet expressed only in cells with maternal nuclear DNA content, can differentiate androgenetic complete moles ($p57^{KIP2}$ negative) from partial moles and nonmolar gestations (both $p57^{KIP2}$ positive) [19–21]. DNA ploidy analysis can help distinguish diploid complete moles from triploid partial moles, but it does not differentiate complete or partial molar pregnancies from hydropic abortions (which can be diploid or aneuploid) [15,21].

In late 2005, emerging data regarding the challenges of diagnosing early molar pregnancy prompted the medical director of a large Planned Parenthood affiliate to initiate this retrospective review of all cases of hydatidiform mole diagnosed in first-trimester abortion patients from August 2001 through March 2005. Our primary objective was to assess the accuracy of the initial histopathologic diagnosis of molar pregnancy through independent expert pathology review, flow cytometric ploidy analysis and $p57^{KIP2}$ immunohistochemical staining. We also examined the clinical course of patients through chart review and concerted follow-up efforts.

2. Materials and methods

During the study period of August 2001 through March 2005, the Planned Parenthood affiliate offered surgical abortions up to 19 weeks' gestation at eight clinic sites in Northern California; in January 2001, the affiliate also initiated medication abortion services through 63 days' gestation using mifepristone and misoprostol. All services were provided in accordance with medical standards and guidelines established by the Planned Parenthood Federation of America. The Human Subjects Institutional Review Board at the University of California, San Francisco, approved this study. Although we received no grant funding, the reference laboratory that provided pathology services for the affiliate covered the costs of confirmatory testing.

All patients presenting to the affiliate for first-trimester abortion services underwent medical screening followed by transvaginal ultrasonography for pregnancy confirmation and dating. Trained nurses or medical assistants performed the ultrasound scans, and the attending physician in the abortion service confirmed the results prior to the procedures.

Using their preferred techniques, experienced physicians performed the aspiration abortions by either manual or electric suction. They visualized the uterine aspirate immediately following each procedure using backlighting and, if necessary, a handheld magnifying lens. The tissue was sent for pathologic analysis to the affiliate's reference laboratory (a mid-sized Clinical Laboratory Improvement Amendments-certified and College of American Pathologist-accredited laboratory specializing in women's health care) if the physician suspected a gestational abnormality such as ectopic or molar pregnancy and in all cases of aspiration for management of complications. Patients were scheduled for a routine follow-up visit in approximately 2 weeks. If the pathology report returned with a diagnosis of hydatidiform mole, however, the patient was referred promptly to a specialist for evaluation and hCG surveillance.

Advanced practice clinicians and physicians administered medication abortion services at the affiliate. The regimen used during the study period included mifepristone 200 mg administered orally at the health center followed by home administration of misoprostol 800 mcg vaginally. Patients returned for transvaginal sonography approximately 2 weeks postmifepristone to assess the success of the procedure. Because the abortion process occurred at home, tissue was not examined unless the patient required uterine aspiration for treatment of failed or incomplete abortion.

In mid-2001, the affiliate began using a computerized risk management database (Doctor Quality Risk Prevention and Management System, Quantros, Inc., http://www.quantros.com/srm.htm) to track adverse events, including molar pregnancy. Methods of ascertainment included urgent and routine follow-up visits, voluntary reports by patients or health care providers, and review of medical records and pathology reports. When complications were treated off-site, affiliate staff requested medical records and, if necessary, made at least three attempts to contact the patient to assess her condition.

We examined the risk management database to identify all cases of hydatidiform mole diagnosed by histopathologic examination in first-trimester abortion patients between August 1, 2001, and March 31, 2005. The reference laboratory compared the affiliate's case list against its own database of pathology reports to ensure complete ascertainment of cases. We extracted information from all available medical records on patient characteristics, clinical presentation, the abortion procedure, tissue examination results, patient follow-up and outcomes. We attempted to reach the referral physician or hospital to obtain missing information regarding postevacuation management and outcomes. If follow-up information remained incomplete, we attempted to contact the patient to assess her clinical course and, when indicated, to encourage her to return for further hCG surveillance.

The affiliate's reference laboratory sent the tissue blocks from patients diagnosed with hydatidiform mole to the Department of Pathology at the Keck School of Medicine, University of Southern California (USC), for review by an independent pathologist with expertise in GTN and for immunohistochemical staining with antibody to $p57^{KIP2}$. The USC clinical laboratory performed flow cytometric ploidy analysis. One of the authors (JCF, chief of OB-GYN Pathology at USC) reviewed all test results (initial pathology