Human Pathology (2013) **44**, 2861–2864

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Human PATHOLOGY

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Case study

Ovarian complete hydatidiform mole: case study with molecular analysis and review of the literature☆,☆☆

Jennifer K. Sehn MD[a,*], Lindsay M. Kuroki MD[b], Margaret M. Hopeman MD[b], Ryan E. Longman MD[b], Colleen P. McNicholas DO[b], Phyllis C. Huettner MD[a]

[a]*Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO, 63110, USA*
[b]*Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, MO, 63110, USA*

Received 30 May 2013; revised 7 June 2013; accepted 19 July 2013

Keywords:
Ectopic pregnancy;
Complete mole;
Hydatidiform mole;
Ovary;
STR

Summary Ectopic complete molar pregnancy in the ovary is an exceptionally rare event. Here we present a case of ovarian complete hydatidiform mole in a 20-year-old gravida 2 para 1 woman. At presentation, the patient underwent excision of a hemorrhagic left ovarian cyst, with routine sections demonstrating a hemorrhagic corpus luteum with a single microscopic focus of detached atypical trophoblast, without chorionic villi. Subsequent left salpingo-oophorectomy for persistently elevated human chorionic gonadotropin led to a final diagnosis of complete hydatidiform mole arising in the ovary. The fallopian tube was unremarkable. Zygosity was determined using short tandem repeat analysis, confirming the diagnosis of monospermic complete mole. In the clinical setting of a markedly elevated human chorionic gonadotropin level and an ovarian mass, histopathologic examination is critical in distinguishing ectopic pregnancy from choriocarcinoma. Short tandem repeat analysis can be a useful adjunct to histologic diagnosis in challenging cases.

1. Introduction

The incidence of molar ectopic pregnancy is estimated to be 1.5 per 1,000,000 births [1]. Complete mole occurring in an ovarian ectopic pregnancy is vanishingly rare, with an estimated incidence of 1 in 50 million pregnancies, represented by only 13 cases reported in the literature since 1925 [1-13]. Complete molar pregnancy arises from fertilization of an empty ovum by 2 sperm (dispermic 46XY, 10% of all complete molar pregnancies) or by a single sperm followed by duplication of the haploid paternal complement (monospermic 46XX, 90% of complete moles). Approximately 20% of patients with complete mole require chemotherapy for persistently elevated serum human chorionic gonadotropin (hCG) levels after removal of the molar tissue, and 2% to 3% of patients develop gestational choriocarcinoma [14]. Here we report a case of ovarian ectopic complete mole with molecular analysis and review of the literature.

2. Clinical history and pathology

A 20-year-old gravida 2 para 1 woman presented to the emergency department with a 7-day history of heavy vaginal

☆ Conflicts of interest: The authors have no conflicts of interest to declare.

☆☆ Sources of support: Funding for molecular analysis of this case came from the Department of Pathology and Immunology of Washington University in St. Louis, St. Louis, MO.

* Corresponding author. Washington University School of Medicine, Department of Pathology and Immunology, Campus Box 8118.
E-mail address: jsehn@path.wustl.edu (J. K. Sehn).

0046-8177/$ – see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.humpath.2013.07.027

bleeding and abdominal pain. Her hCG level was markedly elevated at 100,355 mIU/mL. Transvaginal ultrasonography demonstrated a 3.0 × 2.7 × 2.2–cm complex left adnexal mass, with free fluid in the pelvis. No intrauterine pregnancy was identified. The patient underwent diagnostic laparoscopy with excision of a hemorrhagic cystic mass that was adherent to the left ovary and pelvic sidewall. The specimen was submitted entirely for histologic examination, which showed a single microscopic focus of atypical trophoblast along with a hemorrhagic corpus luteum. No other benign or malignant germ cell elements were identified. Choriocarcinoma could not be ruled out because of trophoblast atypia and the absence of chorionic villi.

After discharge, the patient again presented on postoperative day 11 with persistent vaginal bleeding and abdominal pain. The serum hCG level at this time was elevated above the preoperative level, at 100,680. Transvaginal ultrasonography showed enlargement of the complex adnexal mass, with no evidence of a gestational sac. Subsequently, the patient underwent laparoscopic left salpingo-oophorectomy. Gross examination of the specimen showed an unremarkable fallopian tube and a 5.5 × 4.1 × 2.5–cm aggregate of hemorrhagic, fragmented ovary with a prominent corpus luteum. Intraoperative frozen sections showed atypical trophoblast with no chorionic villi. Routine histologic sections showed an ectopic complete hydatidiform mole of the left ovary, with markedly enlarged, irregular villi with central cisterns, surrounded by abundant, circumferential atypical trophoblast proliferation (Fig. 1). The patient was followed with serial measurement of quantitative serum hCG levels until undetectable.

3. Materials and methods

Ovarian tissue was macrodissected from 5 unstained formalin-fixed, paraffin-embedded, 5-μm tissue sections. Molar trophoblast and villi were macrodissected from 20 unstained formalin-fixed, paraffin-embedded, 5-μm sections. DNA was extracted from both samples using the QIAamp DNeasy Blood and Tissue Kit (Qiagen, Valencia, CA) according to the manufacturer's instructions, including optional RNAse treatment. DNA extracts were assessed for purity and quality using a spectrophotometer (NanoDrop, Wilmington, DE), fluorometer (Qubit, Grand Island, NY), and gel electrophoresis. Short tandem repeat (STR) microsatellite analysis was performed on 0.5 ng of input DNA following the protocol for the PowerPlex 16 HS assay kit (Promega, Madison, WI). Briefly, 15 STR loci and the amelogenin locus (used for sex determination) were amplified by multiplex polymerase chain reaction with fluorescent labeling. Capillary electrophoresis analysis was performed with an Applied Biosystems 3730xl DNA Analyzer using GeneMapper 4.0 software (Applied Biosystems, Grand Island, NY), followed by manual review of the STR peaks.

4. Results

The ovary and products of conception showed differential allelic profiles at 14 of 16 evaluated loci, with no evidence of aneuploidy in the molar tissue (Fig. 2). Only 1 allele was present for each locus in the molar tissue. Two loci were uninformative, meaning that the single allele present in the molar tissue was also present in the ovarian tissue (ie, the mother and the father carry the same allele), including the X chromosome at the amelogenin locus. These STR findings confirm the diagnosis of a monospermic complete hydatidiform mole, showing duplication of a single set of paternally derived alleles with absence of a maternal genetic contribution.

5. Discussion

Ectopic complete mole of the ovary is vanishingly rare, with our case being only the 14th reported since 1925. Previous reports occurred in 25- to 46-year-old women,

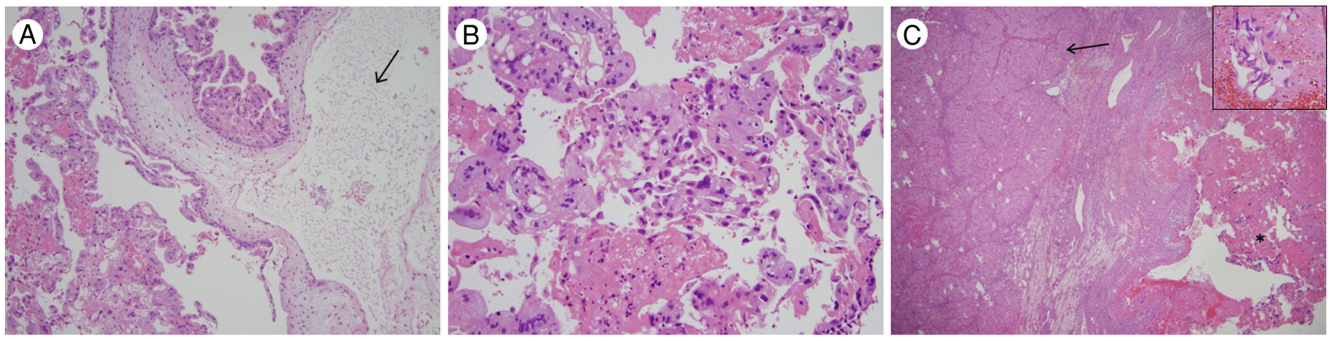

Fig. 1 Microscopic findings. A, Histologic sections of the left ovary show massive, edematous villi with central cisterns (arrow) and circumferential trophoblast proliferation. B, Trophoblast shows marked atypia. C, A large corpus luteum (arrow) is seen in the ovarian parenchyma adjacent to atypical trophoblast (asterisk), which is highlighted in the inset.