Case Reports and Reviews

Case Report

Placental Site Choriocarcinoma, Vanishing Twin And Polycystic Ovary Syndrome

Donna K Hobgood

Erlanger Women's Institute for Specialized Health, UT College of Medicine, Chattanooga Units, 1751 Gunbarrel Road, Chattanooga, Tennessee 37421, USA

Correspondence

Donna K Hobgood

Erlanger Women's Institute for Specialized Health, UT College of Medicine, Chattanooga Units, 1751 Gunbarrel Road, Chattanooga, Tennessee 37421, USA

E-mail: donnahmd@gmail.com

- Received Date: 01 Nov 2022
- Accepted Date: 06 Nov 2022
- Publication Date: 10 Nov 2022

Copyright

© 2022 Authors. This is an open- access article distributed under the terms of the Creative Commons Attribution 4.0 International license.

Abstract

Background: Polycystic ovary syndrome (PCOS) is a common endocrinopathy causing both metabolic syndrome and cancer risks.

Case: This patient presented with PCOS including dysfunctional uterine bleeding, obesity, and hypothyroidism. Genetic evaluation revealed no specific findings other than probable PCOS in her mother, and review of her past history showed presence of non-metastatic choriocarcinoma in her placenta.

Conclusion: This patient was the surviving twin whose vanishing twin was a probable hydatidiform mole resulting in choriocarcinoma of placental site facilitating testosterone crossing the placenta to cause androgenization.

Teaching Points

Vanishing twin can be considered a risk factor for polycystic ovary syndrome in surviving twin. Since polycystic ovary syndrome is not diagnosed until after puberty, history of vanishing twin can give an extra emphasis on early prevention of the many serious sequelae of this condition.

Introduction

Polycystic ovary syndrome is a common multifactorial polygenetic condition with many health implications in a spectrum of severity. Early detection would add impetus to preventive strategies such as childhood weight control [1]. Hyperandrogenic state during fetal period [2-6] has been implicated.

Criteria for diagnosis are oligomenorrhea, hyperandrogenism, and polycystic ovary morphology [7,8]. Varying combinations of these criteria are noted and have been found to show linear correlations with clinical severity of obesity, insulin resistance, circadian rhythm biomarkers, and serum levels of androgens, anti-Mullerian hormone (AMH) and luteinizing hormone (LH).

Many genes have been associated with polycystic ovary syndrome and appear to be pleiotropic for lipid metabolism, androgen and various receptor activities, and menarchy and menopause timing [9]

Strong evidence is extant that fetal exposure to androgens is the common mechanism of polycystic ovary syndrome [2-4]. Testosterone exposure increases anti-Mullerian hormone (AMH) activity which further downstream results in polycystic ovary syndrome [5]. The effects of AMH include insulin resistance, obesity, diabetes, hirsuitism, resistance to ovulation [10] and thus the follicular ovary pattern of increased estrogens and testosterone and increased risks for uterine, ovarian and breast cancer seen in women with polycystic ovary syndrome [11,12].

Case report

A 20 year old female was followed in gynecology clinic since menarchy at age 14 with heavy erratic vaginal bleeding. Additional problems were developmental delay, learning difficulty, extreme obesity, insulin resistance, hypothyroidism, chronic gastrointestinal complaints of abdominal and pelvic pain, nausea, vomiting, diarrhea, constipation, difficulty sleeping, depression, asthma, attention deficit disorder and vitamin D deficiency. Depo-provera and birth control pills were used intermittently with some improvement in menstrual control. Labs were positive for an LH/FSH ratio consistent with polycystic ovary syndrome. Pelvic and abdominal ultrasounds were positive for follicular ovaries and hepatic steatosis. Colonoscopy and upper endoscopy showed erosive esophagitis. Formal genetic evaluation was sought by her endocrinologist who suspected Prader-Willis syndrome.

Citation: Hobgood DK. Placental site choriocarcinoma, vanishing twin and polycystic ovary syndrome . Case Rep Rev. 2022;2(2):1-3.

The geneticist's evaluation included female karyotype, no evidence for Prader-Willis, or for fragile X syndrome or for any other abnormality.

Medications are medroxyprogesterone 150 mg every three months, promethazine 25 mg tablet one three times daily after meals, synthroid 120 mg tablet daily, omeprazole 40 mg capsule daily, hyoscyamine 0.125 mg one-two every 4 hours for cramping in abdomen, singulair 10 mg nightly, albuterol 2.5 mg/3 mil (0083%) nebulizer solution as needed, cetirizine 10 mg prn allergies, fluoxetine 20 mg daily, naproxen 250 mg twice daily, ondansetron 8 mg disintegrating tablet as needed for nausea, and metamucil plus calcium daily.

Physical exam reveals effect of pleasant demeanor, normal ambulation, and mild facial hirsuitism, Vital signs are blood pressure 132/78, height 5" (1.524m), weight 300 lbs (136 kg) BMI 56.36 kg/m^2. Axillary exam done in response to patient request to check soreness in her right underarm area shows mild hidreadenitis supporativa.

Pelvic ultrasound showed endometrium 16.3 mm, uterus 7.4x4.7x4.2 cm, right ovary 4.0x2.5x2.3 cm with multiple follicles less than1 cm in size. Left ovary 6.3x4.7x5.7 cm with 3.6 cm cyst with debris and 2.9 cm simple cyst with no fluid in cul de sac present.

Labs showed glucose 108, complete blood count normal, thyroid indicators normal on replacement, lipids normal with cholesterol 168 mg/dl (<200 normal) , HDL 41 mg/dl (>49 normal). LDL 107 mg/dl (<130 normal), non-HDL cholesterol 127 mg/dl (<160 normal), chol/hdl ratio 4.1 (normal 0-5), triglyceride 102 mg/dl (<150 normal), vit D 21 ng/ml (normal 30.0-80.0), normal cortisol free urine, 13 ug/l, cortisol per 24 hours 8ug , urine total volume 650, with creatinine urine 136.97, creatinine per total volume 890 L.

Review of her prenatal history showed that she was the product of an uncomplicated pregnancy other than a history related by patient's mother of vanishing twin on 8 weeks ultrasound at a previous prenatal clinic. Prenatal care began in current clinic at 20 weeks gestation with no abnormalities noted on ultrasound and an anterior placenta documented. Prenatal course was otherwise normal except for a mild febrile illness. She was born by c section for prolonged bradycardia at 6 cm dilation at 39 weeks weighing 7 pounds and 21 centimeters in length. Apgars were normal, and normal neonatal course was noted.

Her mother had history of abnormal periods, mild obesity and clinical exam suggestive of polycystic ovary syndrome and conceived with this her first pregnancy at age 30 without fertility treatment. She transferred to this practice at 20 weeks gestation and records were not available for any data on earlier serum quant beta hcg levels or for ultrasound documentation of a history that she relates of having had a vanishing twin at 8 weeks.

The placenta was examined by pathologists because of nonreassuring fetal heart rate pattern and revealed choriocarcinoma. Pathology report of gross description of placenta noted a 1.5 cm nodule. Histologic report stated: "The firm tan nodule shows extensive necrosis and proliferation of bizarre trophoblasts, both synsytial and cyto trophoblasts. In some areas there is simply proliferation of these abnormal trophoblasts without any chorionic villi. In some areas it appears to be arising from nonhydropic chorionic villi. The villi also show the appropriate level of maturity. No evidence of villitis is seen.

Serum beta hcg level in mother was 199.3 15 days after delivery, decreasing to 40.6 one week later and to 0 at two months postpartum and 7.0 three month postpartum, 1.7 six months postpartum and 0.3 one year postpartum, to remain at 0 for the next year of follow-up, and was <2 at 14 years postpartum. No evidence of metastasis was noted.

Gynecologic oncologic consultation recommended no need for treatment. She conceived again two years postpartum and delivered a male infant.

The patient did not tolerate breastfeeding nor several formulas but was maintained on Alimentum. The patient was thin until age 4 when she began to gain weight from good appetite. Menarchy occurred at age 14 after which time she was diagnosed with the bleeding issues and other health issues.

The patient has a special education diploma from high school and was home schooled. She lives with her mother, her father and her brother, and functions to perform self-care and some household tasks. Her mother is concerned about her health and is puzzled as to what to do about it.

Discussion

This patient's mother having polycystic ovary syndrome had increased risks for abnormal ovulation and follicullogenesis which manifested as dizygotic twinning where one twin was likely a complete hydaditaform mole that developed into a placental choriocarcinoma [13]. The especially high levels of beta HCG from this pathology

exposed the fetus to higher testosterone levels that were above maternal physiologically high levels on the basis of history of polycystic ovary syndrome [1]. Whereas maternal serum testosterone would not be expected to cross the placental aromatase barrier, maternal high levels of anti-Mullerian hormone on the basis of polycystic ovary syndrome would block the aromatase function, and these extremely high testosterone concentrations would cross into the fetus causing her clinical course. Cystic ovaries and related epigenetic changes from the testosterone exposure in utero caused high levels of steroid hormones with all the downstream effects including anovulation and endometrial hyperplasia and dysfunctional uterine bleeding, receptor changes diffusely including gastrointestinal, endocrinologic, dermatologic, and many associated health effects that are as yet not clearly understood including central nervous system, mood disorders and learning disabilities. In this patient there were all the above sequelae to include learning disabilities as has been found in some but not all patients with vanishing twin syndrome [14-18]

So while genetic assessment of her health status has to date revealed no specific findings, other than likely inheritance of PCOS from her mother, there is evidence that there was an epigenetic mechanism in utero of extreme levels of testosterone from extreme levels of beta hcg having its etiology in choriocarcinoma formed from vanishing twin. Pinpointing the etiology of polycystic ovary syndrome in the patient should lead to better prevention and treatment of the sequelae. For example, if the cause of in utero exposure is high levels of beta human chorionic gonadotropin, diagnosis at menarchy and treatments such as methotrexate, an effective treatment for gestational trophoblastic disease may be considered. Diagnosis prior to puberty may be possible when causes are pinpointed and treatment could include considering pre-pubertal treatments of not only conventional ones like birth control pills or depo-provera injections but also medications such as methotrexate to

block ovarian and extra-ovarian targets where polycystic ovary effects are occurring. Further, the emerging science of gender transformation is increasing knowledge that could possibly relate to the hormonal pattern of polycystic ovary syndrome, and some of this knowledge could be used to modulate the masculinization of the individual with in utero epigenetic exposures which promote polycystic ovary pathologies in genetic females. An extension of this effort is that genetic males at risk for sequelae such as hypospadias and even metabolic syndrome from in utero exposures [19, 20] related to maternal polycystic ovary pathologies may have other pathologies that could benefit from diagnosis and treatment initiation in childhood.

Disclosures of Financial /Funding

None

Acknowledgments

None

Meetings where presented

None.

References

1. Hiam D, Moreno-Asso A, Teede HJ, et al. The genetics of polycystic ovary syndrome: an overview of candidate gene systematic reviews and genome-wide association studies J Clin Med. 2019;8(10): 1606.
2. Sinha N, Roy S, Huang B, Wang J, Padmanabhan V, Sen A. Developmental programming: prenatal testosterone-induced epigenetic modulation and its effect on gene expression in sheep ovary†. Biol Reprod. 2020;102(5):1045-1054.
3. Gur EB, Karadeniz M, Turan GA. Fetal programming of polycystic ovary syndrome. World J Diabetes. 2015;6(7):936-942.
4. Dumesic DA, Goodarzi MO, Chazenbalk GD, Abbott DH. Intrauterine environment and polycystic ovary syndrome. Semin Reprod Med. 2014;32(3):159-65.
5. Raperport C, Homburg R. The source of polycystic ovarian syndrome. Clin Med Insights Reprod Health. 2019;13:1179558119871467.
6. Wang YC, Su HY, Liu JY, Chang FW, Chen CH. Maternal and female fetal virilization caused by pregnancy luteomas. Fertil Steril. 2005;84(2):509.
7. Lim AJR, Indran IR, Kramer MS, Yong EL. Phenotypic spectrum of polycystic ovary syndrome and their relationship to the circadian biomarkers, melatonin and cortisol. Endocrinol Diabetes Metab. 2019; 2(3): e00047.
8. Day F, Karaderi T, Jones MR, et al. Large-scale genome-wide meta-analysis of polycystic ovary syndrome suggests shared genetic architecture for different diagnosis criteria. PLoS Genet. 2019; 15(12): e1008517.
9. Song DK, Hong YS, Sung Y-A. Vitamin D receptor and binding protein polymorphisms in women with polycystic ovary syndrome: a case control study. B MC Endocr Disord. 2019 19:145
10. Paredes AH, Salvetti NR, Diaz AE, Dallard BE, Ortega HH, Lara HE. Sympathetic nerve activity in normal and cystic follicles from isolated bovine ovary: local effect of beta-adrenergic stimulation on steroid secretion. Reprod Biol Endocrinol. 2011;9:66.
11. Dilaver N, Pellatt L, Jameson E. et al. The regulation and signalling of anti-Müllerian hormone in human granulosa cells: relevance to polycystic ovary syndrome. A Hum Reprod 2019 Dec 1;34(12):2467-2479.
12. Pierre A, Peigné M, Grynberg M, et al. Loss of LH-induced down-regulation of anti-Müllerian hormone receptor expression may contribute to anovulation in women with polycystic ovary syndrome. Hum Reprod.28(3):762-9.
13. Parikh F, Aher S, Rachabatuni C, Paidhungat JV. Unusual Presentation of Choriocarcinoma JIACM 2005;6(1): 93-4
14. La Sala GB, Villani MT, Nicoli A, Gallinelli A, Nucera G, Blickstein I. Effect of the mode of assisted reproductive technology conception on obstetric outcomes for survivors of the vanishing twin syndrome. Fertil Steril. 2006;86(1):247-249.
15. Anand D, Platt MJ, Pharoah PO. Vanishing twin: a possible cause of cerebral impairment. Twin Res Hum Genet. 2007;10(1):202-209.
16. Hariharan C, Jajoo SS, Khemka AS. A Rare Case of Choriocarcinoma following a normal pregnancy and delivery. International Journal of Recent Surgical and Medical Sciences. IJRSMS 2017;03(01): 064-066
17. Chung C, Kao MS, Gersell D. Incidental placental choriocarcinoma in a term pregnancy: a case report. J Med Case Rep. 2008;2:330.
18. Katsigianni M, Karageorgiou V, Lambrinoudaki I, Siristatidis C. Maternal polycystic ovarian syndrome in autism spectrum disorder: a systematic review and meta-analysis. Mol Psychiatry. 2019;24(12):1787-1797.
19. Schneuer FJ, Bower C, Holland AJ, et al. Maternal first trimester serum levels of free-beta human chorionic gonadotrophin and male genital anomalies. Hum Reprod. 2016;31(8):1895-1903.
20. Siemienowicz KJ, Filis P, Shaw S, et al. Fetal androgen exposure is a determinant of adult male metabolic health. Sci Rep. 2019;9(1):20195.