Case report

Case report of a paraganglioma arising from a mature cystic teratoma of the ovary

Jennifer Haagab,⁎, Lakotah Hardieb, Amber Berningc, Lauren Fishbeind, Bradley R. Corre

division of obstetrics and gynecology, university of colorado anschutz medical campus, aurora, CO, USA
bdivision of endocrinology, metabolism, and diabetes, department of medicine, university of colorado anschutz medical campus, aurora, CO, USA
cdepartment of pathology, university of colorado anschutz medical campus, aurora, CO, USA
division of gynecologic oncology, department of obstetrics and gynecology, university of colorado anschutz medical campus, aurora, CO, USA

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ABSTRACT

Paragangliomas are rare neuroendocrine neoplasms derived from sympathetic or parasympathetic paraganglia and have the ability to secrete catecholamines. We present the case of a 37-year-old asymptomatic female who underwent right ovarian cystectomy for a mature cystic teratoma and was found to have an intra-tumoral paraganglioma. More research is needed to determine metastatic potential as well as the likelihood of recurrence of these unique neoplasms.

1. Introduction

Paragangliomas arise from extra-adrenal chromaffin cells in both parasympathetic and sympathetic paraganglia (Erickson et al., 2001). Sympathetic paragangliomas are unique in their ability to secrete catecholamines, producing symptomatology associated with catecholamine excess in affected patients, including hypertension, episodic headaches, sweating, and tachycardia. However, the production of catecholamines is not a truism and these tumors may exhibit either secretory or non-secretory behavior (Erickson et al., 2001). In contrast, parasympathetic paragangliomas are usually non-functional. The incidence of paraganglioma is rare and often described together with pheochromocytoma, intra-adrenal paragangliomas, with approximately 500–1600 cases in the United States per year (Chen et al., 2010). Although the majority of paragangliomas and pheochromocytomas are sporadic, up to 40% may be associated with an identifiable heritable pathogenic variant (Fishbein et al., 2013).

We report a case of a paraganglioma within a mature cystic teratoma.

2. Case report

The patient is a 37-year-old G3P0030 with past medical history significant for hairy cell leukemia, diagnosed at age 32 and treated with one cycle of cladribine, with no evidence of disease since that time. She was seen in clinic for assistance with conception. She previously underwent embryo banking prior to chemotherapy but subsequently conceived spontaneously. In her first spontaneous pregnancy, trisomy 18 was detected by non-invasive prenatal testing (NIPT) and confirmed by products of conception after dilation and curettage. In her second spontaneous pregnancy, trisomy 21 was detected by NIPT and confirmed by products of conception after dilation and curettage. Her third spontaneous pregnancy was complicated by a missed abortion requiring dilation and curettage with normal pathology. The remainder of her gynecologic history is unremarkable. She has a family history of a maternal aunt with post-menopausal breast cancer, but no family history of ovarian cancer. She also has no personal or family history of kidney stones, hypercalcemia, pancreatic cancer, renal cancer, pituitary tumors, pheochromocytoma, or paraganglioma.

Given the prior miscarriages, the patient elected to undergo in vitro fertilization (IVF). On transvaginal ultrasound prior to frozen embryo transfer in a subsequent attempt at conception, a new 4 cm solid-appearing right ovarian mass was noted. A subsequent MRI done approximately 2 weeks later demonstrated an 8 cm bilobed fat-containing right adnexal mass most consistent with a mature cystic teratoma (dermoid cyst). Tumor markers were drawn and were all within normal limits: CA-125 was 20 U/mL (normal 0–35 U/mL), AFP was 2.9 ng/mL (normal 0.0–9.0 ng/mL), HCG was < 1 IU/L (normal 0–5 IU/L), and LDH was 151 U/L (normal 124–271 U/L). She underwent diagnostic laparoscopy and right ovarian cystectomy, clinically consistent with mature cystic teratoma.

Pathology confirmed a classic mature cystic teratoma of

⁎ Corresponding author at: University of Colorado Anschutz Medical Campus, School of Medicine, 12631 E 17th Ave, B198-6, Aurora, CO 80045, USA.
E-mail address: Jennifer.haag@cuanschutz.edu (J. Haag).

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5 × 5 × 1 cm. Histopathologic analysis demonstrated mature ectodermal, mesodermal, and endodermal components (Fig. 1A). Within the teratoma, there was a separate 4.2 mm area containing cells arranged in nested and corded architecture (Fig. 1B), with epithelioid cells demonstrating amphophilic to basophilic cytoplasm and round nuclei with fine chromatin, consistent with paraganglioma. Supporting immunohistochemical studies demonstrated patchy positivity for chromogranin (Fig. 1C) and CK7, diffuse positivity for synaptophysin (Fig. 1D), and negative staining for TTF-1 and calcitonin. In addition, a Sox10 immunostain highlighted scattered sustentacular cells (Fig. 1E). In total, these findings are consistent with a 4.2 mm paraganglioma arising within a mature cystic teratoma.

Subsequent evaluation consisted of a CT scan of the chest, abdomen, and pelvis which was unremarkable. She underwent additional laboratory testing given the finding of the embedded paraganglioma: plasma metanephrine was 0.15 nmol/L (normal 0.00–0.49 nmol/L), plasma epinephrine was 44 pg/mL (normal 10–200 pg/mL), plasma norepinephrine was 345 pg/mL (normal 80–520 pg/mL), and chromogranin A was 53 ng/mL (normal 0–95 ng/mL), all within normal limits.

Four months after the initial surgery, the patient was noted to have a recurrent right ovarian cyst with a 1.9 cm echogenic right ovarian lesion on transvaginal ultrasound done during IVF evaluation. She underwent a second laparoscopic right ovarian cystectomy and pathology was consistent with a mature cystic teratoma without evidence of paraganglioma. At the most recent follow-up, the patient was eight months out from the initial surgery and without evidence of disease.

3. Discussion

Paragangliomas are uncommon neuroendocrine tumors derived from paraganglia of the parasympathetic or sympathetic nervous system. Paragangliomas can be secreting or non-secreting which can
render the diagnosis challenging. Most are localized but about 15 percent can become metastatic (Erickson et al., 2001; Chen et al., 2010).

Only two previous cases of paranganglioma within a mature cystic teratoma have been reported in the literature (Mahdavi et al., 2003; Elliot et al., 2012). In addition, McCluggage and Young reported a case series of probable primary ovarian parangangliomas but this is likely a separate entity (McCluggage and Young, 2006). Both in our case and the two published cases of paranganglioma within a teratoma, the paranganglioma was only discovered post-operatively on pathology; therefore, no pre-surgical biochemical testing was done. In the case of paranganglioma within a teratoma described by Mahdavi et al., the patient did not present with any symptoms of catecholamine excess. The paranganglioma was 1.0 × 1.1 × 1.2 cm within the teratoma and no recurrence at 36 months (Mahdavi et al., 2003). In the case described by Elliot et al., the size of the paranganglioma and any recurrence information were not given. The patient did have a history of hypertension and tremor, although unclear whether this was related to her paranganglioma as no biochemical data was available and they do not describe if it resolved post-operatively (Elliot et al., 2012). In our case, the patient also had no symptoms of catecholamine excess in retrospect and biochemical testing was normal, but again, they were done after removal of the teratoma.

Up to 40 percent of parangangliomas and pheochromocytomas are hereditary and associated with clinical syndromes, such as multiple endocrine neoplasia type 2 (MEN2), neurofibromatosis type 1 (NF1), von Hippel Lindau (VHL), and hereditary paranganglioma-pheochromocytoma syndromes (Fishbein et al., 2013; Favier et al., 2015; Fishbein, 2016; Else et al., 1993). Because such a high percentage of patients with paranganglioma and pheochromocytoma have an inherited component, it is recommended that all patients with these tumors have clinical genetic testing. In the case presented here, given the complete containment of an extremely small foci (4.2 mm) of paranganglioma tissue within the teratoma which also contained other differentiated tissue, it was felt that this was likely a random event that the cells of the teratoma formed a paranganglioma. Therefore, no genetic work-up or further follow-up specific for the paranganglioma was performed. Full body imaging was performed and showed no other masses or tumors and the patient had no personal or family history suggestive of hereditary conditions associated with pheochromocytoma or paranganglioma. Nevertheless, the patient was instructed to monitor for new diagnosis of hypertension, diabetes, or symptoms of headaches, palpitations, or diaphoresis.

In general, determining metastatic potential and likelihood of recurrence of paranganglioma and pheochromocytoma is difficult for many reasons. Soft tissue or intra-tumoral vascular invasion is a poor predictor of metastasis. Additionally, the time between first diagnosis of paranganglioma and identification of any metastases is highly variable, sometimes up to twenty years. Finally, there is no reliable and widely accepted histologic scoring system to aid in predicting metastatic potential of paranganglioma (Fishbein, 2016). Therefore, all patients who have paranganglioma are recommended to be followed for life to monitor for recurrence, additional primary tumors, or metastatic disease over time (Fishbein, 2016). Although this patient had a recurrence of her dermoid cyst, no paranganglioma was identified in the recurrence, further suggesting the paranganglioma was a random event. Additional research is needed to further characterize this unique occurrence of paranganglioma within a mature cystic teratoma.

4. Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Credit authorship contribution statement

Jennifer Haag: Investigation, Writing - original draft, Writing - review & editing, Visualization. Lakotah Hardie: Investigation, Writing - original draft, Writing - review & editing. Amber Berning: Writing - review & editing, Visualization. Lauren Fishbein: Writing - review & editing. Bradley R. Corr: Conceptualization, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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