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Case report

Yolk sac tumor presenting as a colonic mass in a post-menopausal woman: A case report

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1. Introduction

Ovarian germ cell tumors (OGCTs) account for 20–25 percent of all ovarian neoplasms. However, only 5 percent of these neoplasms are deemed to be malignant (Sagae and Kudo, 2000). Yolk sac tumors are believed to derive from the endodermal sinuses of the primordial yolk sac. These tumors make up approximately 14–20 percent of all malignant OGCTs (Shah et al., 2008). The median age of diagnosis is 19 years, where 40% of cases occur in the prepubertal period (Hannan et al., 2015). It is exceptionally rare for yolk sac tumors to occur in a postmenopausal woman, and therefore, this often makes it difficult to diagnose in this patient population. This article aims to add to better this understanding by supplying a case report of a woman who developed a malignant yolk sac tumor in the postmenopausal period. Here, we report a case of a yolk sac tumor in a postmenopausal patient that presented as a right colonic mass suspicious for appendiceal abscess. We also summarize the pathophysiology and management of malignant germ cell tumors.

2. Case report

A 54 year old postmenopausal female presented to the emergency department reporting a one day history of constant, right-sided abdominal pain and mild nausea. She had not had a bowel movement for four days and did not report passing flatus. She also reported vaginal bleeding for the past three days. Her past medical history was significant for multiple sclerosis, neurogenic bladder, sciatica, and leukoplakia of the tongue. Physical exam demonstrated generalized abdominal tenderness on the right side to palpation without guarding or rebound and was otherwise unremarkable. Rectal and pelvic exam were deferred at this time. Complete blood count and comprehensive metabolic panel were only notable for mild anemia with hemoglobin and hematocrit of 11.5 and 33.6 respectively. A CT scan of the abdomen and pelvis was obtained and significant for a 7.5 low-density mass-like area anterior to the cecum that was concerning for a complex mass or a developing abscess (Figs. 1 and 2). Ovaries and uterus were visualized on this imaging and noted to be normal in appearance. Initially, it was felt that this could be an appendiceal abscess, but the patient reported a history of appendectomy. General surgery was consulted by emergency department and recommended close follow up with outpatient evaluation and colonoscopy. Patient received oral analgesics which improved her pain and was discharged in stable condition. Colonoscopy was arranged and findings revealed no polyps or tumors, no inflammatory changes, and no anorectal pathology. Due to persistent pain and concern for possible malignancy, the patient was scheduled for diagnostic laparoscopy and mass removal via colorectal surgery service. The patient underwent a robotic assisted radical right hemicolectomy with en bloc resection of portion of retroperitoneum, portion of abdominal wall, and adherent intraabdominal tumor measuring 12 × 5 × 7 cm. Intraoperatively, the mass was visualized and appeared to be arising from the right colon. The cecal mass was very adherent to surrounding tissue structures and necrotic in gross appearance. Female reproductive anatomy was visualized and grossly normal in appearance. The mass was not easily separated from the large bowel and consequently, conversion to

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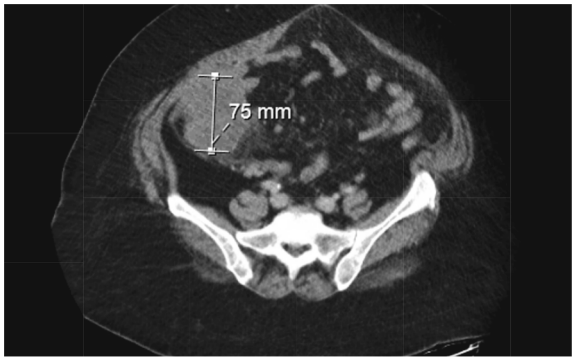

Fig. 1. Noncontrast enhanced CT of yolk sac tumor measuring 75 mm in diameter (axial view).

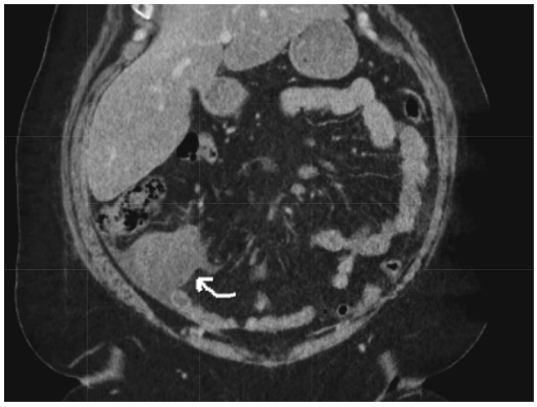

Fig. 2. Noncontrast enhanced CT of yolk sac tumor demonstrating potential involvement of large intestine (transverse view).

laparotomy was performed. Frozen section of mass was sent to pathology and yielded indeterminate results. Multiple excisional biopsies were taken of peritoneal nodules that were also visualized during the case. Final pathology of the gross specimen yielded a yolk sac tumor with clear surgical margins and 13 mesenteric lymph nodes negative for metastatic disease. Tumor did not appear to invade bowel wall or other surrounding female reproductive structures. The patient was then referred to gynecologic oncology. The CT images from the emergency department were reviewed and the endometrium appeared thickened and heterogeneous. Due to this finding and the patient's postmenopausal bleeding, there was concern that the yolk sac tumor was arising from the endometrium. The decision was made to proceed with examination under anesthesia and dilation and curettage. During this procedure, findings were significant for a necrotic mass protruding through a 4 cm dilated external cervical os. The tissue was placenta-like in appearance. The tissue was removed and endometrial sampling was performed. On final pathology, endometrial curettings demonstrated yolk sac tumor staining strongly positive for AFP and CK-OSCAR and weakly positive for CD117 and CD30. The patient was counseled on treatment options with a strong recommendation for platinum-based chemotherapy. She proceeded with two cycles of bleomycin/etoposide/cisplatin (BEP) chemotherapy. Her treatment course was complicated by neutropenia, diffuse tinea cruris, and pulmonary embolism. She was started on anticoagulation. After just 2 cycles, her serologic response of AFP was excellent, decreasing from 30,000 to 12. The patient then underwent an interval hysterectomy and bilateral salpingo-oophorectomy. Final pathology revealed an inactive endometrium with evidence of treatment effect and a lack of evidence for residual yolk sac tumor. The myometrium demonstrated florid adenomyosis and few small leiomyomas. Fallopian tubes were unremarkable, and ovaries demonstrated small inclusion cysts bilaterally. Patient underwent third cycle of BEP with addition of growth factor for NCCN high risk neutropenia. Due to profound weakness, the patient was unable to tolerate four cycles, and therefore, chemotherapy was discontinued. Post-chemotherapy CT demonstrated no evidence of bulk disease. It was recommended that patient is followed for surveillance on every three month basis and is having AFP monitored closely. At six month follow up, the patient was without evidence of disease and her AFP remained normal at 7.

3. Discussion

In this report, we describe a case of metastatic yolk sac tumor arising from the endometrium in a post-menopausal patient. Overall, OGCTs are quite uncommon at an annual incidence rate of 1:100,000. (Bailey and Church, 2005) Most of these malignancies occur in the premenopausal state with an average age at diagnosis of 19 years (Hannan et al., 2015). In the postmenopausal period, there have been only dozens of case reports. Ultimately, this has led to complexities in terms of timely recognition of the malignancy and choices in effective therapy regimens in this population.

Yolk sac tumors characteristically present with mostly clinical manifestations of mass effect. These symptoms include but are not limited to rapid abdominal enlargement, ascites, early satiety, and abdominal pain (Bailey and Church, 2005). Vaginal bleeding is an unlikely finding, though it was one of the primary symptoms of the patient discussed in this report. Because of the vagueness of the symptoms that occur in OGCTs, this can inevitably lead to delay in diagnosis and treatment. The location of the primary malignancy can be variable as well. Most common sites of primary development include the ovary and gonadal ridge. Postmenopausal yolk sac tumors can arise from the endometrium as in this case, but it is rather unusual. When arising from the endometrium, the most common symptom documented in literature is abnormal uterine bleeding. Mentioned symptoms of mass effect are not typically seen with an endometrial primary origin (Sinha et al., 2021). Furthermore, the largest measured metastatic lesion in this case report was found to be on the colon; this is quite uncharacteristic for postmenopausal yolk sac tumors. Yolk sac tumors have a variety of extragonadal sites of development, such as the vagina, brain, mediastinum, retroperitoneum. Most often these extragonadal sites of primary tumor are involved in cases of premenopausal patients (Damato et al., 2016). It is poorly understood if the extragonadal locations change depending on the menopausal status of the patient. In this case, the believed primary location was the endometrium. Because of their rarity, it is not well understood whether yolk sac tumors are more likely to appear with endometrial primary development in premenopausal or postmenopausal women (Sinha et al., 2021).

The pathogenesis of yolk sac tumors developing in the postmenopausal period is poorly understood but believed to differ from premenopausal malignancies. In the premenopausal period, neoplasia arises mostly from endodermal sinus that is not obliterated (Roma and Przybycin, 2014). In the postmenopausal period, the hypotheses of pathogenesis are (1) arrested migration of germ cells during embryogenesis, (2) disoriented migration of germ cells, (3) aberrant differentiation of malignant cells to more embryonic state, (4) differentiation from other somatic carcinoma, and (5) incomplete abortion creating primary tumor site (Euscher, 2019; Salinas et al., 2021). Yolk sac tumors have been reported as either pure or with other cell types. These mixed pathologies have fallen into classifications such as endometrioid/adenocarcinoma, serous carcinoma, uterine sarcoma, clear cell carcinoma, and complex atypical hyperplasia (Salinas et al., 2021). Going forward, understanding the effects of pure versus mixed yolk sac tumor pathology and responses to chemotherapeutics will be vital to improving patient survival rates.

The yolk sac cells classically secrete AFP and keratin, and elevation of these biomarkers is seen commonly in both premenopausal and

postmenopausal patients (Euscher, 2019). The patient of this case report was found to have an initial AFP level of 36,004. AFP can be seen elevated in not only yolk sac tumor, but hepatocellular carcinoma and gastric carcinomas as well (Guo et al., 2015). In patients who present with vague GI/GU symptoms, testing for AFP elevations may aid narrowing of differential diagnosis. Though an elevated AFP level can raise suspicion of possible yolk sac tumor, preoperative values have not been found to be indicative of overall survival. However, it has been found that AFP is useful when used as a surveillance biomarker for yolk sac tumors postoperatively, and higher levels of AFP correlate with decreased five-year survival rates (Guo et al., 2015; de La Motte Rouge et al., 2011).

The gold standard for treatment of all germ cell tumors of the ovary stands to be platinum-based chemotherapy. Specifically, three to four courses of bleomycin, etoposide and cisplatin (BEP) following surgical resection often prevents recurrence (Williams et al., 1994). Patients who underwent surgical resection and platinum-based therapy for malignant germ cell tumors have a five year survival rate of up to 93% (Tewari et al., 2000). However, these treatments are predominantly studied in premenopausal women. Because of the rarity of yolk sac tumors to present in the postmenopausal timeframe, platinum-based chemotherapy is only presumed to be the best chemotherapy regiment when in reality other therapeutics have potential to be a better choice. Furthermore, though highly effective, the BEP regimen can have significant late toxicities including ototoxicity, neuropathy, early-onset cardiovascular disease, and secondary malignant neoplasms. Research on new therapies for germ cell tumors is limited by issues specific to rare tumors, such as lack of clinical trials and small sample sizes. Current studies are looking to substitute carboplatin for cisplatin to reduce toxicities. Other studies are searching for biomarkers that can predict cancer recurrence in patients with germ cell tumors. Specifically, this patient participated in the clinical trial SWOG S1823 which studies micro ribonucleic acid (miRNA) 371 and whether levels can predict recurrence. AFP and hCG are still found to be the mainstay biomarker in terms of response to therapy and recurrence of these postmenopausal yolk sac tumors. Typically, these biomarkers are checked every month for a period of two years and then less frequently over time. Review of symptoms and radiographic imagine is also done every two to four months for the first two years (Salani et al., 2011). However, it could be argued due to the lack of knowledge of yolk sac tumors presenting in postmenopausal women as well as the variability in clinical presentation and pathology, tighter surveillance is merited.

Prognosis of yolk sac tumors are variable. Survival rates of yolk sac tumors are 60–100% in stages I-II vs 50–75% in stages II-IV (Bailey and Church, 2005). Thought often deemed “curable,” as previously mentioned, toxicities from treatment can be lasting and newer, less toxic treatment options should be explored. For patients with isolated recurrent disease, surgical resection of the tumor should be considered. For recurrent disease with persistently elevated tumor markers after first-line chemotherapy, treatment options include paclitaxel, ifosfamide, cisplatin (TIP) or clinical trial if available. Referral to a tertiary care center is highly recommended in this setting.

Yolk sac tumors in postmenopausal female are incredibly rare and poorly understood disease process. Females who have undergone menopause and present with vague abdominal symptoms and/or postmenopausal bleeding should be evaluated promptly with should be evaluated promptly with physical exam and imaging. Based on imaging, patient should also be evaluated with tumor markers as indicated and supportive diagnostics should caution clinicians to consult with a gynecological oncologist for further evaluation. Similar to the clinical trial mentioned in this paper, there are ongoing studies assessing the positive predictive value of MiRNA expression in diagnosis of these tumors (Nappi et al., 2021). With additional case reports of postmenopausal yolk sac tumors, current knowledge of the disease will be strengthened, and surveillance and treatment measures will be better suited for this atypical demographic.

Informed Consent

Case report was discussed with the patient and informed consent was obtained before initiation of case report writing. All protected health information was deidentified.

Author contributions

Riley Short is the primary author who reviewed the case, performed primary literature review, and wrote the manuscript. Dr. Molly Greenwade is the gynecologic oncologist who was the attending physician in this patient’s care and aided in review of the manuscript. Dr. Albert Bonebrake is a gynecologic oncologist who reviewed the case and provided editing of the manuscript.

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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