CASE REPORTS

An Unusual Case of Ascites in a Reproductive Female

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Ascites, an accumulation of fluid in the peritoneal cavity, is commonly caused by liver cirrhosis and only 10% is attributed to malignancy.4 However, if other diagnoses are not considered, delay and mismanagement might ensue. Here we present a 28 year old female with sickle cell trait, obesity, PCOS, and a self-reported recent diagnosis of liver cirrhosis who presented to the ED with severe abdominal
distention, vomiting, shortness of breath, and bilateral leg swelling. Ultrasound and CT scan of the abdomen showed moderate ascites and small dense liver while EGD showed no obvious signs of elevated
portal pressure. Further investigation, including ascitic fluid analysis and in-depth history led to a pelvic ultrasound and endometrial biopsy which confirmed endometrial adenocarcinoma. Images for staging revealed diffuse peritoneal carcinomatosis (Stage 4B). The patient, who was uninsured, was discharged in
stable condition with plans to initiate urgent chemotherapy pending Medicaid approval. A high degree of suspicion for alternative causes of ascites may be necessary, especially in cases such as this young, non-
alcoholic female with laboratory and endoscopic results that do not support the ascites coming from decompensated liver cirrhosis. Moreover, with increasing incidence of endometrial carcinoma diagnosis, more thorough evaluation of abnormal uterine bleeding is appropriate, especially if high risk factors (metabolic syndrome, nulliparity) are present.

BACKGROUND

Ascites, the pathological fluid accumulation within the peritoneal cavity, commonly accompanies gynecologic, hepato-renal, and gastroenterological diseases. Initial investigation is directed to liver disease or other GI disorders.[1, 2] However, cancer accounts for 10% of cases of ascites. Of these, 80% are epithelial in origin, including ovarian and endometrial carcinomas.[2] In 2023, greater than 66,000 new cases of uterine cancer were diagnosed, of which 80% were endometrial adenocarcinoma, making it the most prevalent malignancy of the female reproductive organs.[3]

Uterine cancer is most frequently diagnosed among women aged 55–64, with a median age of 63. However, more than 20% of cases occur in younger individuals, especially in non-Hispanic black women, who have a mortality rate 2-fold higher than other races and ethnicities.[4,5]

CASE REPORT

A 28-year-old uninsured, nulliparous, African American woman with a past medical history of abnormal uterine bleeding (AUB) and a recent diagnosis of liver cirrhosis from an outside facility presented to the emergency department with shortness of breath and abdominal distension. The patient reported that the ascites was secondary to liver cirrhosis and had received one paracentesis treatment.

Approximately 1 year prior to consult, the patient noted abdominal cramps often causing her to "curl up into a ball". She had longer menstruation period intervals from her baseline, and worsening menorrhagia. Birth control pills had only minimally improved the symptoms. Interval history showed persistence of symptoms along with notable generalized weakness, easy fatigability, increased hours of sleep, and decreased appetite.

Four (4) months prior, the patient had quit her job due to increased bloating and prominent abdominal distention. The patient reported that a liver ultrasound was done, and that she was diagnosed with liver cirrhosis. A month later, the patient underwent her first paracentesis, removing 5 liters of fluid from her abdomen. Symptoms continued to worsen causing the patient significant emotional stress. She was eventually started on escitalopram by her primary care physician (PCP). The patient decided to seek reevaluation and presented to our medical facility, in the neighboring county from her residence.

Initial laboratory tests at our institution showed normocytic anemia, acute renal failure, normal liver function tests, normal coagulation tests, and a slightly elevated proBNP. CT of the abdomen and pelvis showed moderate ascites with body wall edema associated with portal venous hypertension and small dense liver. Ultrasound of the abdomen showed small cirrhotic liver and very large volume ascites. Initial paracentesis yielded approximately 16 liters of olive-colored cloudy fluid. EGD was performed and did not demonstrate evidence of portal hypertension.

Further review of history disclosed abnormal vaginal bleeding lasting for approximately 6 months. A transabdominal and transvaginal pelvic ultrasound showed prominent endometrium extending into the endocervical region. A cytologic exam of the ascitic fluid came back positive for malignant cells, most likely metastatic carcinoma of Mullerian origin. An endocervical curettage was unremarkable and an endometrial biopsy revealed endometrial endometrioid adenocarcinoma, FIGO grade 2. Imaging for staging, including MRI, showed diffuse greater omental and peritoneal membrane carcinomatosis. Additional tests including MMR, BRAF, and MLH1 promoter hypermethylation to evaluate for Lynch Syndrome pointed to a sporadic cause. The patient was discharged with a port in place for outpatient, systemic chemotherapy.

DISCUSSION

Ascites is a common complaint which is most often a presentation of decompensated alcoholic liver cirrhosis. It is, arguably, not immediately linked to endometrial cancer (EC). Malignancy as an etiology might be overlooked unless the patient is already diagnosed with cancer, since ascites typically develops in the setting of recurrence and/or advancement of cancer.

EC, occasionally, could be asymptomatic,[6] but most commonly presents as AUB. This patient developed AUB almost a decade prior to the diagnosis of her cancer. In the reproductive age group, along with ruling out pregnancy, STI, vitamin deficiencies, and coagulation disorders, we usually attribute AUB to hormonal imbalance. In a young patient, AUB is generally managed conservatively by surveillance with or without hormonal therapy, risking an inappropriate pause in assessment of this symptom.

Retrospective cohort studies, including those of Grubman and of Soliman,[7, 8] highlight that the work-up of AUB is critical in allowing earlier diagnosis of EC which consequently translates to its timely management; these studies found that most patients diagnosed with EC had incomplete AUB workup years prior to diagnosis. A complete AUB workup in reproductive-aged patients, as recommended by ACOG, includes a pelvic exam, use of progestin-containing therapy, and consideration of a pelvic ultrasound to look for structural causes of AUB and to check the endometrial thickness. An endometrial thickness of 8mm is more likely to be indicated with endometrial biopsy (EMB) in premenopausal uterine bleeding. However, endometrial thickness varies with phases of the menstrual cycle, which would affect this decision.

Additionally, studies also show that relying mainly on endometrial thickness could underestimate the need for a more invasive work-up such as an EMB. Study by Kim, et al in 2016 revealed that a simple measurement of endometrial thickness has a limited role in predicting EC in healthy premenopausal and perimenopausal women with and without AUB and that EMB should be considered if TVUS shows endometrial abnormality including not only a thickened endometrium, but also an endometrial mass, or an endometrial stripe abnormality. Studies also confirm that even with access to health care, many patients with AUB are undermanaged. Moreover, these studies underscore the importance of considering endometrial sampling if patients are considered high risk (obesity, age greater than 45, and/or with bleeding unresponsive to medication/requiring transfusion) in the timely diagnosis of EC.

Several studies already confirm the link of these factors to EC. A retrospective cohort study by Soliman,[8] et. al in 2005 of patients diagnosed with EC treated at MD Anderson Cancer Center from 1989 to 2003 found that many patients diagnosed with EC at younger than 50 years of age were obese (BMI

> 30) and nulliparous. The review by Yang et al. (2019) describes the role of metabolic syndrome in the pathogenesis EC, detailing the molecular and metabolic mechanisms underlying the obesity–EC link. Elevated levels of blood glucose, insulin, insulin-like growth factor, and triglycerides, as well as other molecules associated with metabolic syndrome, can accelerate the progression of EC by acting directly on tumor cells and by remodeling the tumor immune microenvironment. The study also describes the increased risk EC in diabetic patients (2.12x higher compared to the general population), with BMI of more than 25 (2.45x higher), and who are hypertensive (3.5x) as well as the close relation of this so called "triple syndrome of EC" to the incidence and adverse prognosis of EC. A retrospective study on pre- and postmenopausal women with EC by Manap, et.al (2002)[9] in Malaysia determined that there was higher incidence of obesity, younger age at menarche, lesser parity, and a higher number of nulliparous women in the premenopausal group compared to the postmenopausal group. Again, these results argue for expedited endometrial samplings for cancer screening, especially with the up-trending incidence of EC and the risk that the longer interval to diagnosis and treatment is strongly associated with increased mortality and morbidity.

Race and ethnicity should also be factored in when assessing the need for a more invasive diagnostic work-up. A simulated cohort done by Romano and Doll[10] in 2021 assessed ACOG's recommended threshold of endometrial thickness (ET), which is 4mm or greater, to consider EMB or uterine D and C in women with postmenopausal bleeding. Their results show that, among US black women, this threshold missed more than 50% of cases and had 8 times the false negative results compared to the general population. The study showed that ET can be distorted by the presence of fibroids—which are present in approximately 80% of Black women—and that ET measurement is less accurate for diagnosing type 2 EC (non-endometrioid histology, seen in about 30% of Black women). Additionally, a larger proportion of women with type 2 EC were found to have thinner endometrial linings. The study also revealed that 8.3% of patients screened negative—meaning the endometrium was visualized and invasive follow-up was deemed unnecessary—yet were later found to have EC. However small this percentage may seem to be, it is still considered unacceptable when this population of Black women are at the highest risk for aggressive, fast-growing EC. This shows that TVUS as primary evaluation for EC likely disproportionately underperforms for Black women, introducing further opportunity for care delay and care gaps for this group. The same study also concurs with previous studies on the relationships of social factors, including insurance status, and delayed health care diagnosis and undermanagement, solidifying the need to reflect on the current practice pattern of AUB workup.

CONCLUSION

How do the lessons in this case fit in our real-world practice as primary care physicians? In addition to conducting a thorough patient history and maintaining vigilance against diagnostic bias, this unusual presentation of endometrial carcinoma with ascites emphasizes the need to consider endometrial biopsy in premenopausal, nulliparous individuals presenting with longstanding and persistent AUB particularly those with risk factors such as metabolic syndrome. It highlights the importance of adhering to current AUB workup recommendations and considering social, racial, and ethnic factors that may affect diagnostic thresholds.

Further research is needed to develop a more comprehensive approach to evaluating AUB, with an emphasis on early detection strategies for high-risk populations, especially as the incidence of EC continues to rise. Currently, there is no established screening method or preventive strategy for EC in premenopausal women. Investigational efforts—such as the use of a tampon-based detection method (Mayo Clinic Gynecology) and PA-1-mediated biomarker studies (UT Health San Antonio MD Anderson Cancer Center)—are ongoing but not yet clinically available.

Finally, this case adds to the growing call for the inclusion of menstrual health in preventive care, particularly as a means of identifying gynecologic malignancies at an earlier, more treatable stage.

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