Adenocarcinoma Arising in a Three Millimeter-Thick Endometrium

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Numerous papers have recommended nonintervention for postmenopausal bleeding when the endometrial thickness on transvaginal ultrasound is four millimeters or less because the reported risk of endometrial cancer is very low. A case of adenocarcinoma arising in a three millimeter thick endometrium is presented. Occasionally, clinical judgment and suspicion are important in caring for the patient despite recommended guidelines and protocols.

Case Report

A 60-year-old white female gravida 4 para 4004 postmenopausal for five years presented with bleeding of 10 months duration. Past medical history was significant for chronic hypertension and obesity. Physical examination revealed an obese, wellnourished white female in no apparent distress, measuring 5' 7" in height and weighing 210 pounds. The vagina was lined with old blood. The cervix was normal. The uterus was normal size and mobile without any adnexal masses. Pelvic ultrasound showed a uterus measuring 7.6 by 4.7 by 3.8 cm with an endometrial thickness of 3 mm. Office endometrial biopsy was grossly bloody and insufficient. Dilatation and curettage under hysteroscopic guidance was performed in the operating room with pathological findings, "well to moderately differentiated endometrial adenocarcinoma." She was referred to a gynecologic oncologist for staging and further treatment. A robotic total laparoscopic hysterectomy with bilateral salpingo-oophorectomy and pelvic and periaortic lymph node dissection were performed without complication.

Discussion

Transvaginal sonography is a non-invasive tool used to evaluate the endometrium in women with postmenopausal bleeding to assess the risk of malignancy.¹⁻²² Adenocarcinoma of the endometrium is the most common gynecologic malignancy^{1,3,16,19} and the fourth most common malignancy overall in women.³ There are more than 41,000 cases of endometrial adenocarcinoma annually resulting in more than 8,100 deaths.¹ Postmenopausal bleeding is the most common presenting symptom and is "endometrial cancer until proven otherwise."^{1,19} Most women with adenocarcinoma of the endometrium present with vaginal bleeding.^{1,9,16} Postmenopausal bleeding is defined as resumption of bleeding after 12 months of amenorrhea. Postmenopausal bleeding necessitates a workup including evaluation of the endometrium.¹ Most cases of postmenopausal bleeding are from endometrial atrophy,¹ and up to 14% of these women with bleeding have cancer.^{1,2,13,19}

Transvaginal sonography has been used to evaluate the endometrium for about 20 years and has become an acceptable means of assessing the risk of malignancy.^{1-5,9,13-22} The endometrium may act as a biomarker for estrogen stimulation, since estrogen makes the endometrium thicker.¹⁴ Studies have shown that endometrial thickness 4 mm or less on transvaginal sonography in women with postmenopausal bleeding have a low risk of endometrial cancer of about 1 in 1000.^{1,3,11,15,22} Therefore, it has been suggested that these women do not need an endometrial biopsy or dilatation and curettage.¹ The normal postmenopausal endometrium is usually 0.5 mm in thickness and rarely more than 3 mm.⁶ As the thickness of the endometrium

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increases, the risk of developing adenocarcinoma increases.^{2,16} Reports of mean thicknesses of endometrial carcinomas range from 15.2 mm to 20 mm.^{1,3,4} In endometria in which measurement of thickness cannot be obtained, there is a high risk of cancer.⁹ In postmenopausal patients without bleeding, endometrial thickness by transvaginal sonography greater than 11 mm should prompt tissue sampling, but not in less than 11 mm thickness without bleeding.¹⁰

There are reports of endometrial cancer arising in endometria that are less than 5 mm in thickness.⁵ In an Italian study, there were two cases of endometrial cancer in women who had an endometrial thickness less than 4 mm.⁵ Gull et al reported a single case of endometrial cancer in a woman with postmenopausal bleeding whose endometrium was less than 4 mm.¹³ In a select group of Jamaican females, 50% of the cases of endometrial cancer was present in endometria 3-4 mm in thickness.¹⁵

Summary

Postmenopausal bleeding needs some type of assessment of the endometrium.¹ Transvaginal sonography is a non-invasive tool used to evaluate the endometria in women with postmenopausal bleeding to assess the risk of malignancy.¹ Most cases of endometrial cancer arise in endometria that are greater than 5 mm in thickness. There are isolated reports of endometrial cancer arising in endometria that are less than 5 mm in thickness. This is an important case that fell outside the recommended guidelines. Sometimes clinical judgment trumps guidelines and protocols for effective patient care and follow up.

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References

- Goldstein SR. The Role of Transvaginal Ultrasound or Endometrial Biopsy in the Evaluation of the Menopausal Endometrium. *Am J Obstet Gynecol*_{*} 2009;July:5-11.
- Williams SC, Lopez C, Yoong A, McHugo JM. Developing a Robust and Efficient Pathway for the Referral and Investigation of Women with Post-Menopausal Bleeding Using a Cut-Off of <4 mm for a Normal Thickness. *British Journal of Radiology*. 2007;80:719-723.
- Canavan TP, Doshi NR. Endometrial Cancer. American Family Physician. 1999;59(11):1-10.
- 4. Symonds I. Ultrasound, Hysteroscopy and Endometrial Biopsy in the

Investigation of Endometrial Cancer. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 2001;15(3):381-391.

- Ferrazzi E, Trio V, Zannoni E, Filiberto S, Dordoni D et al. Sonographic Endometrial Thickness: A Useful Test to Predict Atrophy in Patients with Postmenopausal Bleeding. An Italian Multicenter Study. *Ultrasound Obstet Gynecol.* 1996;7:315-321.
- 6. Osmers RGW, Kuhn W. Endometrial Cancer Screening. *Current Opinion* in Obstetrics and Gynecology. 1994;6:75-79.
- Brockbank EC, Ghaem-Maghami S, Bridges JE. The Gynecological Management of Women on Tamoxifen: A National Questionnaire Study. *Journal of Obstetrics and Gynaecology*. 2004;24(6):675-679.
- Ayodele OE, Bello TO, Odewale MA, Efuntoye AT. Endometrial Thickness in Asymptomatic Postmenopausal Nigerian Women with and Without Hypertension. *Int J Gynecol and Obstet*. 2006;92:165-166.
- Epstein E, Valentin L. Managing Women with Post-Menopausal Bleeding. Best Practices & Research Clinical Obstetrics and Gynaecology. 2004;18(1):125-143.
- Smith-Bindman R, Weiss E, Feldstein V. How Thick is Too Thick? When Endometrial Thickness Should Prompt Biopsy in Postmenopausal Women Without Vaginal Bleeding. *Ultrasound Obstet Gynecol*. 2004;24:558-565.
- Rozenberg S, Auvertin S, Ham H. A Survey of Physicians' Attitude Towards Women with Postmenopausal Bleeding. *Maturitas*. 2001;39:189-193.
- Van den Bosch T, Vandendael A, Van Schoubroeck D, Lombard CJ, Wranz PAB. Age, Weight, Body Mass Index and Endometrial Thickness in Postmenopausal Women. *Acta Obstet Gynecol Scand*. 1996;75:181-182.
- Gull B, Karisson B, Milsom I, Granberg S. Can Ultrasound Replace Dilation and Curettage? A Longitudinal Evaluation of Postmenopausal Bleeding and Transvaginal Sonographic Measurement of the Endometrium as Predictors of Endometrial Cancer. *Am J Obstet Gynecol.* 2003;188(2):401-8.
- Sit ASY, Modugno F, Hill LM, Martin J, Weissfeld JL. Transvaginal Ultrasound Measurement of Endometrial Thickness as a Biomarker for Estrogen Exposure. *Cancer Epidemiol Biomarkers Prev.* 2004:13(9):1459-65.
- Phillip H, Dacosta V, Fletcher H, Kulkarni S, Reid M. Correlation Between Transvaginal Ultrasound Measured Endometrial Thickness and Histopathological Findings in Afro-Caribbean Jamaican Women with Postmenopausal Bleeding. J Obstet and Gynaecology. 2004;24(5):568-72.
- Schmidt T, Breidenbach M, Nawroth F, Mallmann P, Beyer IM, Fleish MC, Rein DT_Hysteroscopy for Asymptomatic Postmenopausal Women with Sonographically Thickened Endometrium. *Maturitas*. 2009;62:176-178.
- Domingues AP, Lopes H, Dias I, De Oliveira CF. Endometrial Polyps in Postmenopausal Women. Acta Obstetricia et Gynecologica. 2009;88(5):618-20.
- Ozsener S, Ozsaran A, Itil I, Dikmen Y. Endometrial Pathology of 104 Postmenopausal Breast Cancer Patients Treated with Tamoxifen. *Eur J Gynaec Oncol.* 1998;19(6):580-3.
- Nutis M, Garcia KM, Nuwayhid B, Mulla Z, ElMasri W. Use of Ultrasonographic Cut point for Diagnosing Endometrial Pathology in Postmenopausal Women with Multiple Risk Factors for Endometrial Cancer. J Reprod Med. 2008;53:755-59.
- Pansini F, De Paoli D, Serra MM, Campobasso C, Levato F, Giulini D. Combined Use of Progesterone Challenge Test and Endometrium Thickness Evaluated by Transvaginal Ultrasonography in the Preventive Management of Postmenopausal Women. *Gynecol Obstet Invest.* 1992;34:237-239.
- Al-Kadri HM, Al-Awami, Madkhali AM. Assessment of Risk Factors of Uterine Cancer in Saudi Patients with Postmenopausal Bleeding. *Saudi Med J.* 2004;25(7):857-861.
- Opolskiene G, Sladkevicius P, Valentin L. Ultrasound Assessment of Endometrial Morphology and Vascularity to Predict Endometrial Malignancy in Women with Postmenopausal Bleeding and Sonographic Endometrial Thickness > 4.5mm. Ultrasound Obstet Gynecol. 2007; 30:332-340.

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