INCIDENTAL FINDINGS IN GYN ULTRASOUND: WHAT DO YOU DO?

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PHYSICAL EXAM

- Inspection
- Palpation
- Auscultation
21st CENTURY MEDICINE

- Patient intake forms of historical information scanned into an EMR
- Imaging studies
Virtually every organ
• MRI
• CT
• PET
• Ultrasound
MY THESIS

The sensitivity of imaging modalities has been so refined...
MY THESIS

...that we are seeing structures either never before appreciated...
MY THESIS

...or sometimes appreciated but not with such precision.
As we see more and more detail, the response to what we see...
MY THESIS

...has often been based on old and thus preconceived notions...
and not on newer well designed studies to determine the prevalence of various findings and their clinical significance
LET ME USE MY AREA OF EXPERTISE AS AN EXAMPLE
THE VAGINAL PROBE HAS REVOLUTIONIZED GYNECOLOGY
SONOMICROSCOPY

Vaginal sonography provides a degree of image magnification that is as if we were doing ultrasound through a low power microscope.
The ease of performing transvaginal ultrasound (TV U/S) and its increasing use has resulted in an explosion of uncovering incidental findings that are much more common than previously realized.
SO...IS THE SENSITIVITY OF IMAGING TOO GREAT?
No not really
It is the APPLICATION of these findings that has been problematic.
Information obtained with such advancingly refined technology cannot simply be handled according to old preconceived concepts. New studies must be performed before clinical decisions and recommendations may be made.
We must be careful not to overinterpret those findings that may be much more common and less ominous than previously believed. This lecture will cover a variety of situations where we need to learn to “sit on our hands”
So what about simple cystic masses (not ovaries) either palpated or discovered incidentally
Where are we today and how did we get here?
IN THE BEGINNING...
1971

"THE PALPABLE POSTMENOPAUSAL OVARY SYNDROME"
“An ovary that would be considered normal sized in a premenopausal woman should be considered abnormal in a postmenopausal woman…”
“... and probably harbors a tumor not necessarily malignant but not functional or dysfunctional.”
"Patients with palpable postmenopausal ovary syndrome should not be followed of re-evaluated but must be investigated promptly for the presence or absence of an ovarian tumor..."
“... the only method of diminishing the mortality from ovarian cancer is the acceptance of more liberal indications of surgery.”

Barber, 1984
When first introduced, ultrasound showed cystic changes so easily people applied this technology to the old concept of this PPMO Syndrome.
LEFT OVARY
77 Y/O
UNCHANGED OVER 4 YEARS
LT OVARY
POST MENOPAUSE
1989
Often ovarian cancer does not present clinically until the advanced stages. In the past, the presence of any cystic adnexal enlargement in postmenopausal women was an indication for surgical exploration. The ultrasound scans of 42 postmenopausal women with simple adnexal cysts were reviewed. We included only patients who were available for follow-up and who had cysts that were less than or equal to 5 cm in maximum diameter, unilocular (i.e., without septations or solid components), and without ascites. Of these patients, 26 underwent prompt surgical exploration. All exhibited benign histopathology. In 16 patients, serial sono- graphic surveillance was performed every 3–6 months. Two of these patients had exploratory laparotomy at 6 and 9 months of observation; the first operation, for increasing size and septation, demonstrated a cystadenofibroma, and the second, for increasing pain, demonstrated a degenerating myoma. The remaining 14 patients were followed from 10–73 months without any change in size or character of the cyst. Small (less than 5 cm), unilocular postmenopausal cysts had a low incidence of malignant disease (0%) in this series of 28 surgical specimens. Therefore, serial ultrasound follow-up without surgical intervention may play a role in the clinical management of such patients. (Obstet Gynecol 73:8, 1989)
“We concluded that small ($\leq 5$ cm) unilocular, unilateral postmenopausal adnexal cystic masses, with no septations or ascites will have a very low incidence of malignant disease...”
CONCLUSIONS (1989)

“...therefore serial ultrasound follow-up without surgical intervention may play a role in clinical management of such patients.”
1992
ADNEXAL CYSTS in Postmenopausal women
Levine, Gosink, Wolf et al, (Radiology, 1992;184:653)

- 184 asx. women scanned with TV U/S
- 17.3% had simple adnexal cysts
Cysts < 10 cm in asymptomatic post menopausal women > 50 years

- 7705 women scanned, 236 (3.3%) had unilocular cystic adnexal masses
  - 49% resolved in 60 days, 51% persisted
  - 45 women operated, none malignant
- (32 cystadenomas)

CRUCIAL Take Home Message...

- Unlike cervix (dysplasia), breast (DCIS, LCIS), and endometrium (hyperplasias) where I spend much of my day as a clinician looking for "precancers" BEFORE they become malignant....
CRUCIAL Take Home Message…

- ...there is no evidence that this is true in epithelial ovarian cancer
- In other words benign cystadenomas do not BECOME cystadenocarcinomas
- If they did we would have to remove all of these simple cystic structures since 2/3 are consistently shown to be cystadenomas
UNILOCULAR OVARIAN CYSTS (University of Kentucky Ovarian Cancer Screening Program)

- 2763 (18%) had unilocular cysts

Of 2763 women with cysts, ultimately 10 (0.3%) were later diagnosed with cancer. But none of those 10 cancers arose IN the unilocalcular cysts!!

2010
Prevalence, incidence, and natural history of simple ovarian cysts among women >55 years old

Greenlee RT, et al. AJOG April 2010

- PLCO (Prostate, Lung, Colorectal, and Ovarian) cancer screening program

- 15,735 women aged 55-74 underwent TV U/S

- Scanned initially and then yearly for 3 additional years
14% of women had a simple cyst.
32% resolved the following year (presumably few were functional)
In previous cyst free women 8% developed a cyst per year for 3 years, equally distributed through all age groups
Women whose initial U/S had a cyst did not have any increased risk of subsequent ovarian cancer (9/2217 or 0.41%) compared with their counterparts with no cysts (55/12,638 or 0.44%; p=0.85)

This is almost identical to the University of Kentucky screening program data.
CONCLUSIONS: SIMPLE ADNEXAL CYSTS IN PM WOMEN

1) NOT ALL CYSTIC ADNEXAL STRUCTURES ARE OVARIAN IN ORIGIN

2) NONE OF WHAT WE SEE (AT LEAST THOSE WITH SURGICAL CONFIRMATION) ARE "FUNCTIONAL" OR "PHYSIOLOGIC" CYSTS

3) VAGINAL PROBE WILL IDENTIFY MANY SMALL SONOLUCENCES (6-18%)

4) STUDIES WITH SURGICAL CONFIRMATION INDICATE THAT THE INCIDENCE OF SUCH SIMPLE CYSTS BEING MALIGNANT APPROACHES ZERO
CONCLUSIONS: SIMPLE ADNEXAL CYSTS IN PM WOMEN

- Of those with pathology confirmation about 2/3 are serous cystadenomas
- No evidence that BENIGN epithelial ovarian tumors TRANSFORM into malignant (in other words cystadenomas do not become cystadenocarcinomas)
14 radiologists, gynecologists, pathologists, gyn oncs, REIs met for 1 1/2 days in Chicago.

Panel concluded that in PM women:

- Simple cysts <1cm are clinically inconsequential, may or may not be reported at MDs discretion, and need no F/U.

- Simple cysts >1, but <7cm should be described but statement added that “they are almost certainly benign”. Yearly F/U “at least initially” is recommended.

- Simple cysts >7cm “may be difficult to assess completely with U/S and therefore surgical exploration or further imaging (MRI) should be considered.”
WHAT ABOUT THE ENDOMETRIUM?
POSTMENOPAUSAL ENDOMETRIUM

BIG DIFFERENCE BETWEEN INCIDENTAL FINDINGS AND PATIENTS WHO ARE BLEEDING !!!!
What have health care practitioners HEARD and DONE ?!?
If $\leq 5\text{mm}$ is good then $>5\text{mm}$ must be bad.
But remember this was all done in women WITH BLEEDING
So without any validation women with EM > 5mm ABSENT BLEEDING have been and often still are routinely biopsied.
The endometrial echo revisited: Have we created a monster?

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Transvaginal ultrasound has been explored as an inexpensive, noninvasive, convenient way to indirectly visualize the endometrial cavity. For more than a decade numerous studies have indicated that a thin, distinct, well-visualized echo (<4-5 mm) in postmenopausal women with bleeding is as effective as any diagnostic modality in excluding endometrial cancer (99% negative predictive value). Unfortunately, this is not the same as saying that a thick endometrial echo is pathologic. In fact, the positive predictive value of an echo greater than 5 mm is less than 10% for any disease and only 4% for serious disease (cancer or hyperplasia). No studies validating the clinical significance of a nonthin endometrial echo observed in an incidental imaging study have ever been performed. Because 5 mm has been a “cutoff” for excluding endometrial cancers in women with bleeding, many clinicians have assumed that any findings greater than 5 mm need endometrial sampling to exclude disease. The number of postmenopausal women with quiescent fibroids, or polyps, or heterogeneous uterine echoes for technical reasons (previous scarring, axial uterus) is unknown but not insignificant. Furthermore, if transvaginal ultrasound is to be used, it must be performed appropriately, further recognizing that in a substantial number of patients it may not be possible to obtain technically adequate endometrial assessment. So, although transvaginal ultrasound can be a reliable method of excluding disease in many postmenopausal women with bleeding, the incidental finding of a non-thin endometrial echo has not been investigated and should not automatically trigger a need for formal tissue sampling.

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But the problem is not with the imaging...
It is the INTERPRETATION of the imaging
Consider the following case...
65 y/o woman,
- 14 years since menopause
- Excellent overall health
- On no medications
- Presents to ER with lower abdominal pain
CLINICAL CASE

- Afebrile
- Normal labs (blood and urine)
- ER physician orders CT scan with Dx: “R/O diverticular disease”
CT of pelvis and abdomen: “totally unremarkable except region of decreased attenuation centrally located within the uterus. Recommend transvaginal ultrasound”

Patient has a rather large bowel movement with total resolution of her symptoms.
TV U/S performed: “thickened endometrial echo measuring 11.2mm with some heterogenous echoes. Suggest clinical correlation”

Patient back to usual routine of 1-2 hours of tennis per day (singles, no less)
Patient referred to her gynecologist who attempts suction piston endometrial biopsy in office. She is unable to get into endometrial cavity secondary to a stenotic os.
CLINICAL CASE

- Patient is in excellent health
- Patient has no risk factors for endometrial cancer (no diabetes, hypertension or obesity)
CLINICAL CASE

- Patient is parous but had 2 C/S, the last one 31 years ago.
- Because of inability to get tissue, patient is referred to another clinician in a teaching institution in a metropolitan area for a D&C, hysteroscopy under anesthesia.
CLINICAL CASE

- Despite using fine lacrimal probes and ultrasound guidance the cavity is not successfully entered.
- In fact, it was the impression of the operator that a false channel had been created.
Patient sees gyn oncologist in consultation

Patient undergoes hysterectomy

Final pathology report:
“Submucous myoma, inactive”
What is the point of this case?
In discussing this case with a friend who is a gynecologic oncologist, I remarked how interesting it was that these clinicians felt so obliged to get a tissue sampling on the basis of what they perceived to be an abnormal finding on an imaging study and an incidental finding, at that!
He said he probably also would have wanted endometrial tissue sampling! I found this quite perplexing. I said to him, “Doesn’t the gynecologic oncology community recommend that tamoxifen patients not undergo endometrial sampling unless they have bled? (ACOG Committee Opinion 232, April 2000)
He responded, “Yes that’s correct.” I pointed out that the woman we were discussing was 1) not on a drug that has cancer producing potential (tamoxifen), 2) has had no bleeding in 14 years, 3) has never had breast cancer, and 4) plays tennis 2 hours a day.
I asked, why did he feel so obliged to sample HER endometrium since he felt Tamoxifen pts should be left alone UNLESS they bleed? A look of realization slowly came over his face and he said “I guess I see your point.”
So: 1) how common is a thick EM echo in non bleeding patients?

2) when present what is its significance?
Few good prospective studies exist but consider this...
10% of postmenopausal women trying to enroll in the Raloxifene uterine safety studies had asymptomatic endometrial polyps on sonohysterography

A. Parsons (verbal communication)
17% of 550 newly diagnosed postmenopausal breast cancer patients in Brussels had unsuspected asymptomatic polyps prior to initiating tamoxifen therapy.

A randomly selected Danish population aged 20-74 underwent TV U/S and SIS

- Prevalence of uterine polyps overall = 7.8%
- Prevalence increased with age
- In PM women (n=169) prevalence of Asx polyps was 13.0% (n=22)

Dreisler et al Ultrasound Obstet Gyencol 2009:33-102
WHAT IS THE RISK OF MALIGNANCY IN SUCH POLYPS?

- Removed 117 polyps in PM women without bleeding
- NONE were malignant
- Discussed importance of distinguishing EM carcinoma with polypoid growth from carcinoma arising in a polyp (base and surrounding EM must be benign)

- 300 consecutive women with polyps who underwent hysteroscopic removal
- Combined peri and PM patients
- 73 (24.3%) were asx and polyps were discovered incidentally
- ALL asx polyps were benign
1152 Asx PM women diagnosed with a polyp by SIS underwent hysteroscopic removal

- 1 EM cancer in a polyp (<0.1%),
- Mean diameter 40 mm
- 3 perforations, 7 cervical tears, 3 false passages
- 3 cancers (0.3%) occurred in Asx PM wpmen that were not in polyps but were polypoid appearing on imaging and not global
Lev-Sagie A et al, BJOG 2005;112:379-382

- 82 postmenopausal women with incidental sonographic findings of EM “thickening”
- Operative hysteroscopy
- 67 (82%) inactive polyps, 7 submucosal myomas, 6 atrophic EM, 1 proliferative EM, 1 polyp with simple hyperplasia
- NO complex hyperplasia or carcinoma
- 3.6% total complication rate (2 perforations, 1 difficult intubation)
U/S detection of Asx EM cancer in PM women offers no prognostic advantage over Sx disease discovered by uterine bleeding


- 190 women with EM cancer dx AFTER bleeding (symptomatic)
- 123 PM women with “suspicious” U/S on screening…of which 16 (13%) were ultimately dx with EM cancer
- Through 55 months of follow-up overall survival and disease free survival were the same when treatment was undertaken within 8 weeks of bleeding episode
Thus for the negligible risk that an Asx polyp MIGHT harbor a cancer (<1 in a 1000), or < 4 in a 1000 if you include “polypoid growth”, there is no therapeutic or prognostic advantage over waiting until it results in bleeding; and such an approach would spare the other 996 out of a 1000 any intervention and its risks, discomfort and expense.
SO …IN POST MENOPAUSAL BLEEDING…

- “CANCER UNTIL PROVEN OTHERWISE”
- ROLE OF HIGH NEGATIVE PREDICTIVE VALUE OF A THIN DISTINCT EM ECHO
- PERFORM TV U/S FIRST, SONOHYSTEROGRAPHY IF NECESSARY, TO TRIAGE PTS TO 1) NO PATHOLOGY 2) GLOBAL PROCESS (BLIND BX) 3) FOCAL PROCESS (DIRECT VISION)
BUT...FOR AN INCIDENTAL FINDING OF EM THICKENING...

- There is NO validation whatsoever that these patients need AUTOMATIC EM sampling.
- The incidence of thick EM echo is probably 10-17% and is much like “simple” cyst of the post menopausal ovary was 20 years ago.
- Still appropriate (and always was) to use clinical JUDGEMENT if high risk (obese, diabetic, hypertensive, nulliparous).
In the 1980’s EM fluid collection (on transabdominal U/S) was felt to be an ominous sign, very highly associated with malignancy (75% !!)
Postmenopausal Endometrial Fluid Collections Revisited: Look at the Doughnut Rather Than the Hole

STEVEN R. GOLDSTEIN, MD

Objective: To report 30 postmenopausal women and the thickness of the tissue surrounding an endometrial fluid collection seen on vaginal probe ultrasound.

Methods: During routine ultrasound-enhanced bimanual examination, nine postmenopausal women with unremarkable palpation findings and no history of bleeding were found to have endometrial fluid collections. The patients were 9–24 years postmenopausal. All underwent prompt endometrial sampling. Each woman had some degree of cervical stenosis as judged by the operator. At curettage, all had scant tissue, which was reported by the pathologist as “inactive endometrium.”

Results: Ultrasound scans on each patient were reviewed, and it was found that the endometrium surrounding the fluid was uniformly 3 mm thick or less. Subsequently, 21 additional patients with small endometrial fluid collections have been seen. Eight of these had thin endometrium peripherally and were followed conservatively for 6–26 months. Six cases resolved and 12 remained unchanged. Three patients had a thickened heterogeneous endometrium peripheral to the fluid collection. In one, D&C was unsuccessful in two attempts because of cervical stenosis, and hysterectomy was performed. A 1.5-mm endometrial polyp was found. Two other patients with thickened endometria surrounding the fluid had D&C, and hysteroscopy revealed simple hyperplasia without atypia.

Conclusions: Normal atrophic postmenopausal endometrium in association with cervical stenosis can produce endometrial fluid collections, seen easily on vaginal probe ultrasound. If the endometrial tissue surrounding the fluid is thin (3 mm or less), the endometrium is invariably inactive and sampling is not necessary. If the peripheral endometrium is thicker than 3 mm, sampling is mandatory because the tissue cannot be expected to be inactive. Thus, the presence or amount of fluid is not as important as the thickness and character of the surrounding tissue. (Obstet Gynecol 1996;83:738–40)

The presence of an endometrial fluid collection has been thought to be an ominous sign often associated with malignancy. In 1982, Breckenridge et al.1 found that 16 of 17 patients with intrauterine fluid collections on ultrasound had carcinoma in the uterine corpus or cervix. With the development of improved transabdominal resolution, McCarthy et al.2 reported in 1986 that six of eight patients with postmenopausal endometrial fluid collections had benign processes. The vaginal probe affords a degree of image magnification that results in low-power “sonomicroscopy.” Fluid is easily seen in follicular changes of the ovary, in the cul-de-sac after ovulation, or increasingly within the endometrial cavity of postmenopausal women.

I postulated in 19911 that fluid collections seen in the endometrium of many postmenopausal women actually represent transudate associated with cervical stenosis. The purpose of this paper is to report a total of 30 cases of postmenopausal endometrial fluid collections and to describe the need to measure the endometrial tissue peripheral to them.

Materials and Methods

During routine ultrasound-enhanced bimanual examination, nine postmenopausal women with unremarkable palpation examinations were found to have endometrial fluid collections (Figure 1). None had any history of bleeding and none were on hormone replacement therapy. The patients were 9–24 years postmenopausal. The equipment used was either an Aloka 635 5-MHz curvilinear vaginal probe (Corometrics, Wallingford, CT) or a Siemens Sonoline SL1 5–7.5 MHz mechanical sector probe (Siemens Quantum, Issaquah, WA).

Because of concern that the endometrial fluid signaled an abnormality,1,2 each woman had endometrial sampling. There was some degree of cervical stenosis...
POST MENOPAUSE
NO BLEEDING
MORE EMERGING ISSUES RAISED BY THE INCREASED SENSITIVITY OF TV U/S...
ADENOMYOSIS

- Defined as the presence of endometrial glands and stroma ectopically located in the myometrium
- Results in hypertrophy of myometrium and enlargement of the uterine corpus
Incidence depends on how hard you look
- With 3 routine sections in hysterectomy specimens = 31%
- With 6 sections = 61%

CAN result in pelvic pain, uterine enlargement, and heavy abnormal uterine bleeding BUT most often asymptomatic
SONOGRAPHIC DIAGNOSIS CHARACTERIZED BY …

- Asymmetric uterine wall enlargement (in the absence of fibroids)
- Ill defined hyper and hypoechoic areas
- Small anechoic cysts between 1 and 6 mm throughout the myometrium
SONOGRAPHIC DIAGNOSIS CHARACTERIZED BY ...

- Linear striations radiating into the myometrium
- Color Doppler imaging showing radial arteries running straight rather than the typical circular vascularization of fibroids
PROBLEM WITH SENSITIVITY OF IMAGING

- Prevalence of adenomyosis is very high
- "sonomicroscopy" can identify lesions
- If such patients are labeled with a "disease" AND if symptoms develop SUBSEQUENTLY (i.e. perimenopausally) those sx will be BLAMED on the adenomyosis and surgery may be undertaken when it may well be INCIDENTAL and not be causal!
WHAT ABOUT SMALL MASSES WHOLLY CONTAINED WITHIN AN OVARY THAT ARE INCIDENTAL AND ASYMPTOMATIC?
DOES EVERYONE NEED SURGERY?

- Endometriomas
- Dermoids
PROMINENT UTERINE VESSELS
LT ADNEXA

DX AS HYDROSALPINX
PARAOVARIAN CYSTS
NABOTHIAN CYSTS
ADHESIONS
WHILE WE’RE ON THE SUBJECT OF ADHESIONS...
Transvaginal ultrasound is a form of “sonomicroscopy”

The pelvis often contains findings that have not been appreciated before (simple postmenopausal cysts, quiescent PM polyps, asx adenomyosis, small dermoids or endometriomas wholly contained within ovaries, filmy adhesions, Nabothian cysts, paraovarian cysts, PM endometrial fluid collections, etc)

IN SUMMARY
IN SUMMARY...

• Just because we can image something not usually present does not mean it is clinically relevant
• Information obtained with increasingly refined technology cannot be handled with old principles
• “Above all else, do no harm…”
• My personal credo? “Over surveillance, under treat”