Pseudolipomatosis Affects Specimens From Endometrial Biopsies

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Abstract

Pseudolipomatosis refers to optically clear vacuoles that artifactually contaminate specimens, and it most commonly affects the gastrointestinal tract. Pseudolipomatosis closely resembles adult white fat and is of group “A” or “B” when vacuoles have mild or marked variation in size, respectively. Pseudolipomatosis has yet to be reported to occur in the endometrium. Pseudolipomatosis in the endometrium might be easily mistaken for extraterine adipocytes and misdiagnosed as perforation. We retrospectively reviewed 50 consecutive specimens from endometrial biopsies to determine the prevalence of endometrial pseudolipomatosis and whether pseudolipomatosis was related to perforation.

All 50 specimens contained pseudolipomatosis of group “B,” and lacked extraterine tissue. To our knowledge, all patients lacked clinical evidence of perforation at follow-up. Pseudolipomatosis commonly affects specimens from endometrial biopsies and is likely unrelated to perforation. Awareness of pseudolipomatosis is necessary to avoid misdiagnosing uterine perforation.

Collections of variably sized optically clear spaces in specimens from colorectal biopsies were first described in 1985.1 Intestinal gas accumulated during endoscopy was presumed to cause these spaces, although these spaces failed to be reproduced in vitro. This phenomenon was called “pseudolipomatosis” owing to the close histologic resemblance to adipocytes and could be distinguished from adipocytes by the lack of plasmalemmae ultrastructurally. Recent data, including data obtained during a dramatic epidemic, showed that pseudolipomatosis involving the colorectum is likely related to a toxic effect of hydrogen peroxide, a mucosal irritant that is used to sterilize endoscopes, or barotrauma.2,3 Other mechanisms must be involved, however, as pseudolipomatosis cutis occurs in the absence of irritants.4

Pseudolipomatosis has yet to be reported to occur in specimens from endometrial biopsies. Most endometrial biopsies are performed with instruments sterilized with chemical irritants, which might produce pseudolipomatosis by the same mechanism that occurs in the colorectum, and are performed with suction,5 which we hypothesize might contribute to pseudolipomatosis by mixing air with endometrial tissue and by allowing air to contaminate these specimens. Pseudolipomatosis in this setting could be easily mistaken for extraterine adipocytes and lead to a misdiagnosis of perforation. We reviewed a large series of specimens from endometrial biopsies to establish the existence of pseudolipomatosis in this setting and to determine whether pseudolipomatosis was related to perforation. We predicted that endometrial pseudolipomatosis is common and unrelated to perforation.
Materials and Methods

We retrospectively reviewed 4-μm-thick, H&E-stained sections from 50 consecutive formalin-fixed, paraffin-embedded specimens from endometrial biopsies accessioned at our institution during the interval January 4, 2007, to March 6, 2007. All endometrial biopsies were performed to exclude hyperplasia or carcinoma and were performed or supervised by faculty of the Department of Obstetrics and Gynecology at our institution or faculty of satellite clinics of our institution who lacked knowledge of our study. All biopsies were performed with suction and performed in the usual manner. Specimens from curettage were excluded from our study. Clinical suspicion of perforation was obtained from electronic medical records.

All specimens were received completely submerged in 10% buffered formalin and submitted within 24 hours after accessioning for routine processing (Tissue-Tek VIP 5, Sakura Finetek USA, Torrance, CA) Table 1. Pseudolipomatosis was defined similar to previous studies1 as collections of well-circumscribed, optically clear, rounded, variably sized spaces of any diameter that were devoid of plasmalemmae or intervening capillaries. Pseudolipomatosis was classified as group “A” or “B” depending on whether the ratio of the largest vacuole to the smallest vacuole was 4 or less or more than 4, respectively, similar to a previous classification,6 and was quantified arbitrarily as mild, moderate, or severe when pseudolipomatosis involved less than 10%, 10% to 20%, or more than 20% of the volume of the specimens respectively.

Histologic evidence of perforation was defined as the presence of adult white fat, intestinal tissue, or mesothelium.7 Adult white fat was defined as adipocytes, namely, relatively uniform spherical cells measuring 120 μm or less in greatest diameter, with optically clear cytoplasm bound by plasmalemmae, ellipsoidal peripherally placed nuclei, and capillaries at intersections between multiple adipocytes.8 Brown fat was excluded from our study given the unlikely possibility of sampling brown fat via endometrial biopsy.8 All adult white fat was considered to be histologic evidence of perforation for the sake of simplicity and because uterine lipoma, lipoleiomyoma, adenolipoleiomyoma, metaplastic adipocytes, and liposarcoma are rare.7,9,10

To help determine whether pseudolipomatosis might be related to in-house histologic processing, also reviewed were one 4-μm-thick, H&E-stained section each from the thyroid gland, lung, kidney, prostate, urinary bladder, gallbladder, and liver from specimens processed in the same machine.

Results

The ages of the patients ranged from 29 to 81 years. All histologic sections showed adequately fixed and preserved tissue. All 50 specimens (100%) contained pseudolipomatosis. To our surprise, all were classified as group B Image 1, and none were classified as group A. Of the 50 specimens, 21 (42%) had mild pseudolipomatosis, 28 (56%) had moderate pseudolipomatosis, and only 1 (2%) had severe pseudolipomatosis. Some vacuoles were partially filled with fluid or mucus, were optically clear but angulated, or were incompletely circumscribed and failed to meet our strict definition of pseudolipomatosis. Less strict definitions that include such objects as acceptable variants of pseudolipomatosis would increase the number of specimens with severe pseudolipomatosis. Pseudolipomatosis occupied the stroma, mucus, and blood and rarely indented glandular epithelium Image 2. The vacuoles were often separated from each other and sometimes coalesced with each other. Most vacuoles were circular, while some were elongated. Although pseudolipomatosis often appeared identical to colorectal pseudolipomatosis, occasional vacuoles were up to 2.54 mm in diameter and were much larger than those that we have seen affecting the colorectum. Many vacuoles were less than 10 μm in greatest diameter. All specimens lacked adult white fat, intestinal tissue, or mesothelium. Search of electronic clinical notes failed to reveal documentation of any case for which perforation was suspected.

All sections from the thyroid gland, lung, kidney, prostate, urinary bladder, gallbladder, and liver were negative for pseudolipomatosis.

Discussion

In our study of specimens from endometrial biopsies, pseudolipomatosis affected all specimens and was exclusively of group B. Morphologic features of perforation were absent from all specimens, and, to our knowledge, all patients lacked clinical evidence of perforation at follow-up.
Several factors must be considered to determine the etiology of endometrial pseudolipomatosis. Pseudolipomatosis is an artifact thought to be related to a toxic effect of hydrogen peroxide or barotrauma when found in the colorectum and may be related to suboptimal processing, suboptimal fixation, or autolysis when found in the skin. Instruments used for endometrial biopsies are sterilized with chemicals including ethylene oxide (Pipelle de Cornier, manufactured by PRODiMED, Neuilly-en-Thelle, France), which potentially could irritate the endometrium and cause pseudolipomatosis, similar to what is believed to occur in the colorectum. In our study, all endometrial specimens were adequately preserved, and all extrauterine specimens processed in the same machine lacked pseudolipomatosis, so that endometrial pseudolipomatosis is likely related to circumstances other than artifacts of suboptimal processing or fixation. Given that endometrial biopsies are performed with suction, which might mix air within the endometrial cavity with endometrial tissue and allow air to contaminate these specimens, it seems reasonable to conclude that endometrial pseudolipomatosis is at least partly related to air mixing with material from endometrial biopsies. Future studies involving endometrial biopsies performed in the absence of chemical irritants or performed in the setting of frozen sections are needed to definitively determine whether sterilization or processing is linked to pseudolipomatosis.

Pseudolipomatosis potentially can be confused with adult white fat, particularly if pathologists are unaware of the possibility of pseudolipomatosis. Although pseudolipomatosis somewhat resembles fat in that both entities have vacuoles that are optically clear, rounded, and at least focally cohesive, in our study, the optically clear vacuoles were readily classified as pseudolipomatosis by adhering to existing morphologic criteria for fat and for pseudolipomatosis. Specifically, adult white fat contains vacuoles that are relatively uniform in size, spherical, and 120 μm or less in greatest diameter and that surround capillaries, while pseudolipomatosis contains vacuoles that vary greatly in size and are rounded but often not spherical, 2.54 mm or less in greatest diameter, and devoid of intervening capillaries.

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<tr>
<th>Characteristic of Vacuoles</th>
<th>Fat</th>
<th>Pseudolipomatosis</th>
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<tbody>
<tr>
<td>Appearance</td>
<td>Optically clear</td>
<td>Optically clear</td>
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<tr>
<td>Cohesion</td>
<td>Cohesive</td>
<td>Cohesive or discohesive</td>
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<tr>
<td>2-Dimensional borders</td>
<td>Circular</td>
<td>Roudned or circular</td>
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<tr>
<td>Uniformity</td>
<td>Present</td>
<td>Absent</td>
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<tr>
<td>Maximal diameter</td>
<td>≤120 μm</td>
<td>≤2.54 mm</td>
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<tr>
<td>Intervening capillaries</td>
<td>Present</td>
<td>Absent</td>
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<td>Significance</td>
<td>Possible perforation</td>
<td>Artifact</td>
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Despite the fact that fat may rarely be intrauterine, the presence of fat in specimens from endometrial procedures virtually always raises the possibility of perforation and prompts immediate communication between pathologists and clinicians, more complicated clinical follow-up, and consideration of surgical intervention. Awareness of and familiarity...
with pseudolipomatosis, as well as knowledge of the very low rate of uterine perforation, can help pathologists avoid misdiagnosing perforation. Risk of perforation due to endometrial biopsy might be low enough to be considered only a theoretical risk. Perforation rarely follows curettage, including curettage to evacuate incomplete abortion, and uncommonly follows insertion of intrauterine devices.

Conclusions

We performed the first study of pseudolipomatosis occurring in the setting of endometrial biopsies. Pseudolipomatosis affected all specimens and was exclusively of group B. Pseudolipomatosis may be related to irritants used during sterilization or suction during the procedure. Awareness of pseudolipomatosis in this setting can help avoid misdiagnosing perforation.

References