Peripheral hypervascularity of the corpus luteum with ovarian edema (CLOE) may decrease false positive diagnoses of ovarian torsion

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Abstract

Introduction In patients with pelvic pain, corpus luteum with associated ovarian edema (CLOE) may be mistaken for ovarian torsion on ultrasound or CECT.

Methods This was a multi-reader, blinded, retrospective review performed at a single academic center from 2012 to 2018. Cases of CLOE that were misdiagnosed as torsion and cases of ovarian torsion without a lead-point mass were analyzed. Evaluated ultrasound features included presence of a corpus luteum, ovarian and corpus luteum volume, Color Doppler vascularity of the corpus luteum rim compared to that of the ovarian stroma, peripheral follicular displacement, twisted vascular pedicle, and free fluid. Evaluated CT features included presence of a corpus luteum, ovarian and corpus luteum volume, corpus luteum rim enhancement, twisted vascular pedicle, and free fluid.

Results 39 cases of CLOE and 30 cases of ovarian torsion without lead-point mass were reviewed. A corpus luteum was present in 56.7% of torsed ovaries. In CLOE cases, peripheral hypervascularity of the corpus luteum (manifested as enhancement at CECT or flow signal at Doppler US) was present in 67.7% (21/31) of cases on ultrasound, and in 95.7% (22/23) of cases on CT. No peripheral hypervascularity of the corpus luteum was seen in cases of torsion ($p < 0.001$). Torsed ovaries were significantly larger than CLOE cases. Other findings were not significantly different between the two groups.

Conclusion Increased blood flow in the periphery of a corpus luteum on color Doppler ultrasound or on CECT is a strong negative predictor for ovarian torsion.

Keywords Corpus luteum · Ovarian edema · Ovarian torsion · Adnexal torsion

Introduction

Ovarian torsion is a surgical emergency as necrosis, loss of ovarian function, and infertility may result from delayed diagnosis [1, 2]. The most sensitive findings of torsion on

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ultrasound are of ovarian stromal edema (> 95% of cases), which causes ovarian enlargement and peripheral displacement of follicles [3].

Pelvic pain and ovarian edema without torsion is a source of clinical and radiological confusion. Unfortunately, the underlying cause of ovarian stromal edema is not always readily apparent [3, 4]. There are multiple other causes of ovarian edema besides acute torsion, including massive ovarian edema due to partial intermittent torsion [5, 6], malignant involvement of the ovary [7–9], or secondary to inflammation by another adjacent process (such as appendicitis) [10]. A corpus luteum with ovarian edema (CLOE) has been recognized as an alternative cause of ovarian enlargement and pelvic pain, which can mimic ovarian torsion [11, 12]. In a recent study, 12.9% of patients who presented with pelvic pain corresponding to an ovary containing a corpus luteum were misdiagnosed with ovarian torsion [11]. These cases were confused for torsion because of the confounding clinical and sonographic findings, which included ovarian

enlargement and peripherally displaced follicles, and acute pelvic pain corresponding to the enlarged ovaries.

The presence or absence of ovarian blood flow on color Doppler is known to be of dubious significance in the diagnosis of torsion [1], with up to 60% of cases of ovarian torsion having normal blood flow [13, 14] . What has been hypothesized but not previously studied is that the presence of hyperemia around a corpus luteum in the setting of ovarian edema may be a negative predictor for ovarian torsion [11].

This study was designed to evaluate for diagnostically useful differences between cases of surgically confirmed ovarian torsion without an ovarian mass, and cases of CLOE that were prospectively mistaken by the radiologist for ovarian torsion on either ultrasound or contrast-enhanced CT (CECT). Specifically, we tested the hypothesis that in the setting of pelvic pain, demonstration of hyperemia around a corpus luteum may help exclude torsion whether demonstrated on ultrasound or CECT.

Methods

Subjects and imaging

This was a HIPAA compliant and institutional review board exempted retrospective study. A radiology report search tool (Montage, Nuance Communications, Inc.) was used to search ultrasound and CECT studies performed at an academic university hospital from January 2012 to April 2018, using the keywords "ovarian torsion," "adnexal torsion," and "ovary AND torsion." Radiology reports were evaluated for inclusion of ovarian torsion on the differential diagnosis for an enlarged ovary by the prospectively interpreting radiologists, which included both general radiologists and subspecialized abdominal radiologists. While some patients were evaluated with both ultrasound and CECT, this study compared imaging parameters on these modalities separately.

All cases of ovarian torsion were surgically confirmed. Cases of CLOE were proven by lack of ovarian torsion documented in operative reports, or shown clinically by spontaneous improvement with resolution of symptoms. 25.6% of CLOE cases demonstrated resolution of the abnormality on follow-up CT or ultrasound, and none presented with recurrence of pain.

Exclusion criteria for both groups included ectopic pregnancy, presence of an ovarian mass (either on imaging or review of pathology), and presence of another diagnosis associated with enlarged ovaries (such as polycystic ovary syndrome or ovulation induction treatment). Ultrasound studies without transvaginal imaging or adequate color Doppler evaluation were excluded. CT scans obtained without intravenous contrast administration were excluded.

Grayscale and color Doppler ultrasound examinations were performed both trans-abdominally and trans-vaginally. Transvaginal ultrasound was performed with either an 8 or 9 MHz transducer using the Siemens Acuson S3000 Ultrasound System, HELX Evolution.

CT examinations were performed on Siemens Somatom Force, Somatom Definition AS, and Somatom Definition DS scanners. Typical scans were 120 kVp, and mAs were modulated from the topograms. Typical pitch ranged from 0.6 to 0.8, and 5 mm slices were used. Standard intravenous contrast injection was 115 cc Isovue at a rate of 2.4 cc/s. Scans were obtained in the portal venous phase, 70 s after the contrast bolus.

Image analysis and chart review

All included cases were initially evaluated by a radiologist of 5 years' experience in blinded fashion. The diameter of each ovary and corpus luteum was measured in three planes. Care was taken to include the thick-walled rim of the corpus luteum in the volume measurement if a central cystic space was present; extending to the point that ovarian stroma formed a "claw-sign" around the corpus luteum [11]. The volumes of the ovaries and corpora lutea were calculated using the equation for the volume of an ellipsoid: $(\pi/6) \times (\text{Dimension 1} \times \text{Dimension 2} \times \text{Dimension 3})$. A residual volume was obtained by subtracting the volume of the corpus luteum from the overall volume of the ovary. This residual volume was used as a surrogate for ovarian enlargement and edema in order to correct for variable contributions of the corpora lutea to the ovarian volume.

Cases of ovarian torsion and CLOE were randomized into groups of ultrasound and CT cases. Two subspecialty-trained abdominal radiologists of 33 and 17 years' experience were informed of the side and volume of the abnormal ovary, but were blinded to the prospective interpretation and clinical history/outcome. The studies were reviewed on a PACS workstation. In cases of disagreement, a third subspecialty-trained abdominal radiologist of 25 years' experience served as a tiebreaker.

Ultrasound imaging parameters

Imaging parameters evaluated on ultrasound included the presence/absence of a corpus luteum, presence of increased vascularity along the periphery of the corpus luteum on color Doppler, peripherally displaced follicles, twisted vascular pedicle (the whirlpool sign), and free fluid. A corpus luteum was considered to be present if there was either 1) a circumscribed intra-ovarian structure that had diffusely thick walls with crenulated inner margins, with or without a central cystic space, or 2) a circumscribed intra-ovarian structure that was hyperechoic

or hypoechoic relative to the adjacent ovarian stroma, with peripheral vascularity on color Doppler. Increased peripheral vascularity was defined as color Doppler flow in the corpus luteum wall that was greater than that seen within the adjacent ovarian stroma on one or more still images or on a cine clip (Fig. 1). The follicles were considered peripherally displaced if all follicles were along the edge of the ovary, with non-cystic parenchymal stroma centrally. If free pelvic fluid was present, it was characterized as simple or complex.

CT imaging parameters

Imaging parameters evaluated on CECT included the presence/absence of a corpus luteum, peripheral enhancement of the corpus luteum, free pelvic fluid, and a twisted vascular pedicle on the side of the enlarged ovary. A corpus luteum was considered present if there was a circumscribed structure within the ovary that had a uniform peripheral ring of increased attenuation (Fig. 2). The identification of non-enhancing corpus luteum within a torsed ovary on CECT was problematic because it can look identical to a hemorrhagic or necrotic ovary. Thus, the presence of a corpus luteum in these cases was confirmed on concurrent ultrasound if available (Fig. 3). If a corpus luteum was present, a small region-of-interest Hounsfield unit measurement was made along the thick-walled rim.
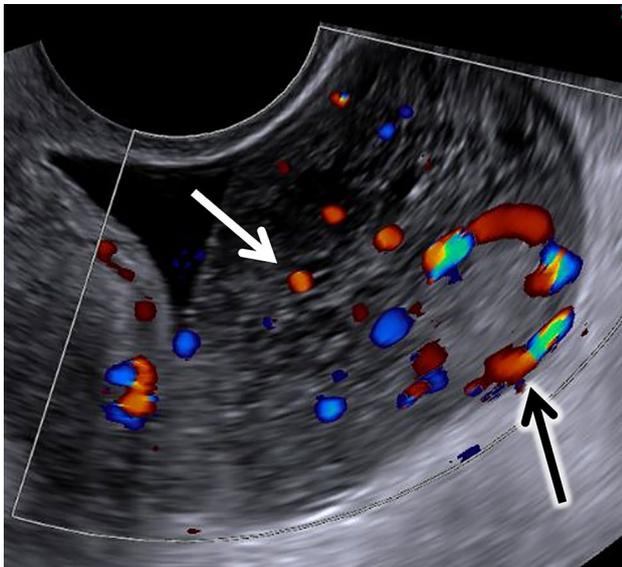

Fig. 2 26-year-old female with CLOE. CECT demonstrating an enlarged right ovary with a rim-enhancing corpus luteum (arrow)

This measurement was made away from the ovarian hilar vessels.

Clinical data

Clinical study parameters including patient's age, pregnancy status, pain acuity, and pain location were obtained from the electronic medical record (EMR). All cases of ovarian torsion were confirmed surgically, and operative notes were reviewed to determine if they underwent detorsion or salpingo-oophorectomy. CLOE case outcomes were obtained via operative reports documenting an edematous ovary without torsion, clinical documentation of spontaneous symptom resolution, and/or resolution of ovarian enlargement on a subsequent ultrasound or CT.

Data analysis

Data analysis was performed using R 2.15 statistical software (R Foundation for Statistical Computing, Vienna, Austria) and Stata 13.0 (StataCorp, College Station, CTX). Participants' demographics, clinical characteristics, and imaging findings were summarized as mean, standard deviation (SD), median, interquartile range (IQR), and range for continuous variables or count (%) for categorical variables, and then compared between patients with CLOE and ovarian torsion. For continuous variables with an approximately normal distribution, t tests were used. Otherwise, Wilcoxon rank sum tests were used. For categorical variables, a Chi squared or Fisher's exact test

Fig. 1 19-year-old female with CLOE. Color Doppler ultrasound image demonstrating an enlarged ovary with peripheral hypervascularity of the corpus luteum (black arrow). The color Doppler signal around the corpus luteum is greater than that seen in the adjacent edematous ovarian stroma (white arrow)
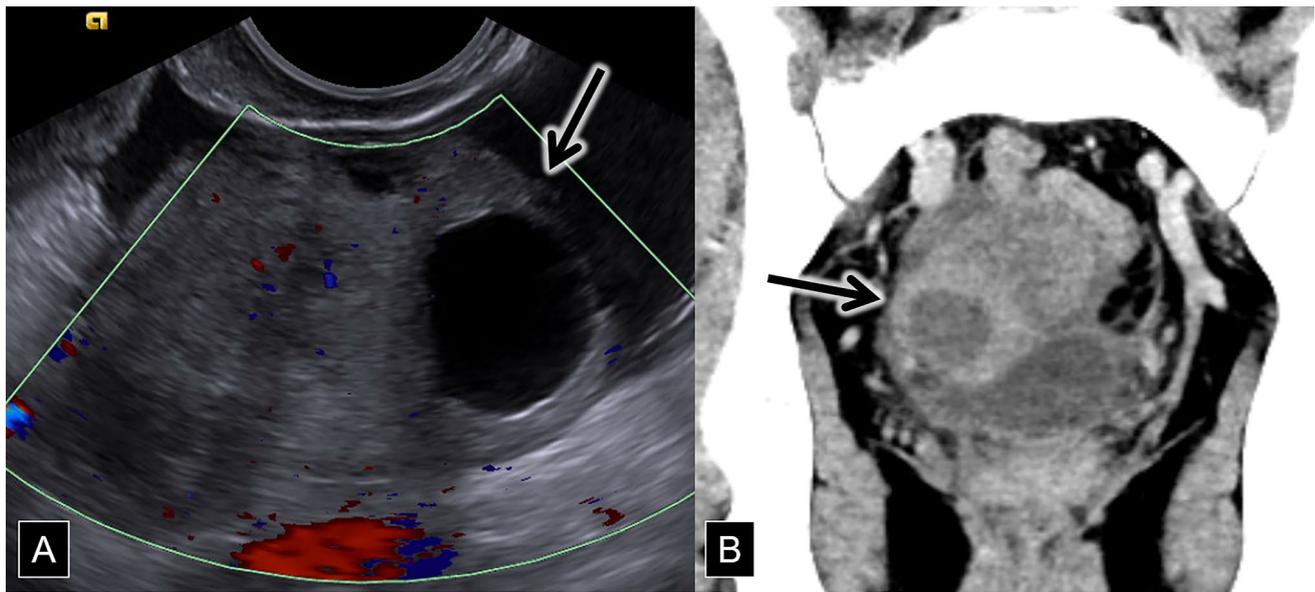
Fig. 3 28-year-old female with ovarian torsion and a corpus luteum cyst. **a** Color Doppler ultrasound imaging demonstrating an enlarged ovary with a corpus luteum cyst (arrow), which does not have periph- eral blood flow. **b** A coronal CECT image shows the enlarged ovary with a non-enhancing corpus luteum cyst (arrow)

(when any expected cell count was less than 5) was used. Unweighted kappa measures were calculated for inter-reader agreement of categorical variables across multiple observers with the exception of ordinal data, where kappa values were calculated using squared (or linear) weights.

Results

The radiology report search resulted in 39 cases of CLOE (31 ultrasounds and 23 CECTs) and 30 cases of ovarian torsion without an ovarian mass (25 ultrasounds and 10 CECTs). 15 cases of CLOE and 5 cases of ovarian torsion were imaged using both ultrasound and CECT. Demographics and clinical features of cases of CLOE and ovarian torsion are shown in Table 1. There were no differences in

Table 1 Demographics and clinical features

	CLOE ($n=39$)	Torsion ($n=30$)	P value
Age (years) mean (SD)	31.5 (8.2)	32.4 (9.5)	
Pregnant	2 (5.1%)	6 (20.0%)	
Presented to ER	33 (84.6%)	26 (86.7%)	
Presented outpatient	6 (15.4%)	4 (13.3%)	
Side (right)	21 (53.8%)	22 (73.3%)	
Side of Pain relative to abnormal ovary			
Same side	25 (64.1%)	30 (100%)	<0.001
Nonspecific	14 (35.9%)	0	
Opposite side	0	0	
Pain Acuity < 1 day	23 (59.0%)	29 (96.7%)	0.002
Underwent Surgery	8 (20.5%)	30 (100%)	<0.001
Detorsion	0	19 (63.3%)	
Salpingo-oophorectomy	0	11 (36.7%)	
Clinical follow-up with pain resolution	31 (79.5%)	0	
Imaging follow-up with normalization	10 (25.6%)	0	

CLOE corpus luteum with ovarian edema

patient age, and all patients in this study were pre-menopausal. The patient's pain corresponded to the side of the abnormal ovary in 100% (30/30) of ovarian torsion cases compared to 64.1% (25/39) of CLOE cases ($p < 0.001$). The remaining 35.9% (14/39) of CLOE cases had generalized pelvic pain. Patients with ovarian torsion presented with pain acuity < 1 day at a higher frequency than patients with CLOE [96.7% (29/30) to 59.0% (23/39); $p = 0.002$].

All cases of ovarian torsion were confirmed during surgery. 36.7% (11/30) had salpingo-oophorectomy, and 63.3% (19/30) underwent detorsion with sparing of the torsed ovary. Since the strongest indication for surgery in a patient with an edematous ovary is the presence of peritoneal signs during physical examination [15], 79.5% (31/39) of CLOE cases were observed with serial abdominal examinations despite concerning imaging findings. 20.5% (8/39) of CLOE cases went to surgery but had no findings of torsion. 25.6% (10/39) of CLOE cases had follow-up imaging, which demonstrated normalization of ovarian size. 79.5% (31/39) of patients with CLOE who did not go to surgery had spontaneous clinical improvement and were discharged.

Ultrasound imaging findings

Ultrasound imaging features are summarized in Table 2. Corpora lutea were identified on ultrasound or CECT in 64.0% (16/25) of patients with ovarian torsion. Ovarian volumes were significantly greater in torsed ovaries compared to cases of CLOE, including median (IQR) ovarian volume [82.0 (56.4, 133.7) to 46.6 (32.8, 68.2) cc; $p = 0.002$], and residual volume (ovarian volume–corpus luteum volume) [56.0 (36.5, 104.8) to 36.7 (25.4, 45.6) cc; $p = <0.001$]. However, there was significant overlap between the two

groups, with the largest CLOE ovary measuring 157.7 cc. Increased vascularity around a corpus luteum on color Doppler was present in 67.7% (21/31) of CLOE cases, and was not present in any case of ovarian torsion (0/25) ($p < 0.001$).

Kappa values for inter-reader agreement: presence of corpus luteum 0.63 (Good); corpus luteum peripheral hypervascularity 0.82 (Excellent); peripheral follicles 0.52 (Moderate); and free fluid 0.72 (Good) [16].

CT imaging findings

CECT imaging features are summarized in Table 3. Corpora lutea were identified in 40.0% (4/10) of cases with ovarian torsion (as confirmed on review of concurrent ultrasound). Median (IQR) residual volume was significantly greater in torsed ovaries compared to CLOE cases [48.8 (37.3, 77.0) to 27.8 (23.3, 36.9) cc; $p = 0.002$]. Peripheral enhancement of the corpus luteum was present in 95.7% (22/23) of CLOE cases, and was not present in any case of ovarian torsion (0/10) ($p < 0.001$). Median (IQR) corpus luteum rim Hounsfield unit measurements were significantly greater in CLOE cases compared to cases of torsion [114.3 (103.9, 127.8) to 52.3 (50.5, 54.4) HU, $p < 0.001$].

Kappa values for inter-reader agreement: presence of corpus luteum 0.67 (Good); corpus luteum enhancement 0.93 (Excellent); and free fluid 0.72 (Good) [16].

Discussion

Failure to diagnose ovarian torsion has potentially catastrophic consequences, including ovarian necrosis and infertility. The presence of ovarian edema is a sensitive finding

Table 2 Ultrasound imaging features

	CLOE ($n = 31$)	Torsion ($n = 25$)	P value
Corpus luteum present	31 (100%)	16 (64.0%)	<0.001
Ovary volume (cc) median (IQR)	46.6 (32.8, 68.2)	82.0 (56.4, 133.7)	0.002
Corpus luteum volume if present (cc) Median (IQR)	9.9 (5.5, 18.9)	18.8 (8.0, 35.8)	
Residual volume (cc) median (IQR)	36.7 (25.4, 45.6)	56.0 (36.5, 104.8)	<0.001
Vascularity within ovarian stroma on color Doppler			<0.001
Absent	1 (3.2%)	14 (56.0%)	
Normal	5 (16.1)	11 (44.0%)	
Increased	7 (22.6%)	0	
Increased vascularity around corpus luteum compared to ovarian stroma	21 (67.7%)	0	<0.001
Peripheral follicles	10 (32.3%)	11 (44.0%)	
Twisted vascular pedicle	0	0	
Free fluid	23 (74.2%)	14 (56.0%)	
Simple	19 (61.3%)	11 (44.0%)	
Complex	4 (12.9%)	3 (12.0%)	

CLOE corpus luteum with ovarian edema

Table 3 CT imaging features

	CLOE (n=23)	Torsion (n=10)	P value
Corpus luteum present	23 (100%)	4 (40.0%)	<0.001
Ovary volume (cc) median (IQR)	37.6 (30.2, 49.1)	58.0 (45.3, 77.0)	
Corpus luteum volume if present (cc) median (IQR)	7.2 (5, 11.9)	15.2 (9.3, 22.4)	
Residual volume (cc) median (IQR)	27.8 (23.2, 36.9)	48.8 (37.3, 77.0)	0.002
Corpus luteum enhancing	22 (95.7%)	0	<0.001
Corpus luteum rim HU median (IQR)	114.3 (103.9, 127.8)	52.3 (50.5, 54.4)	<0.001
Free fluid	17 (73.9%)	6 (60.0%)	
Twisted vascular pedicle	0	1 (10.0%)	

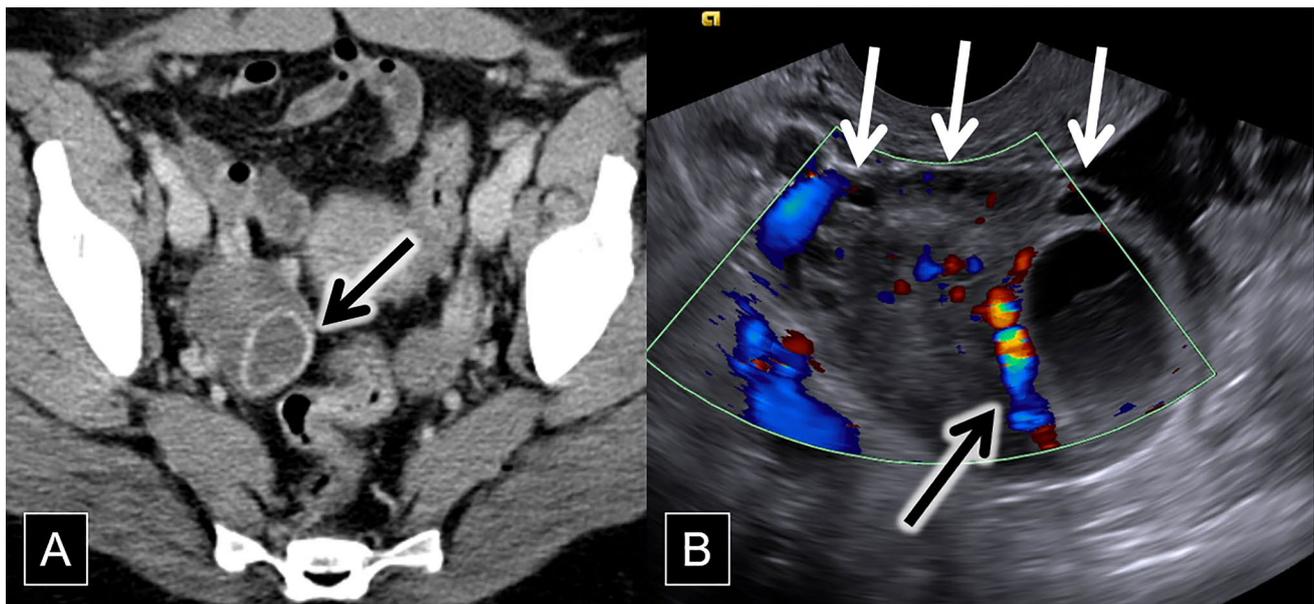*CLOE* corpus luteum with ovarian edema

Fig. 4 34-year-old female with CLOE. **a** Axial contrast-enhanced CT demonstrating an enlarged right ovary with a peripherally enhancing corpus luteum (arrow). **b** Ultrasound imaging demonstrates an enlarged ovary with a corpus luteum (black arrow) and peripherally displaced follicles (white arrows)

in ovarian torsion. However, corpora lutea with associated ovarian edema (CLOE) has been recognized as an alternative cause of ovarian enlargement and pelvic pain that can mimic ovarian torsion (Fig. 4) [11, 17]. Studies have found that 11.1% to 20.2% of patients with suspected ovarian torsion on sonography instead had hemorrhagic corpus luteum cysts discovered during laparoscopy [18, 19]. In ovaries containing a corpus luteum, the ovarian stroma is significantly larger in patients with pelvic pain. However, the development of ovarian edema great enough to cause confusion for ovarian torsion is relatively uncommon and seems idiosyncratic [11].

In this series, 56.7% (17/30) of torsed ovaries had an identifiable corpus luteum without peripheral hypervascularity that is typical of corpora lutea (Fig. 5). The patients with CLOE demonstrated peripheral hypervascularity 67.7% (21/31) of the time on ultrasound, and 95.7% (22/23) of the time on CECT. We suggest that the presence of a corpus luteum with peripheral hypervascularity can be used to reduce false positive diagnoses of ovarian torsion. It is important that this imaging finding should not supersede high clinical suspicion by the surgeon or peritoneal signs, particularly because these may suggest the presence of other undetected indications for surgery (e.g., profusely bleeding ruptured ovarian cysts, appendicitis, or intermittent ovarian torsion). It should also be noted that the converse (lack of peripheral corpus luteum blood flow) is not useful to predict the presence of ovarian torsion, since many normal corpora lutea do not demonstrate this finding.
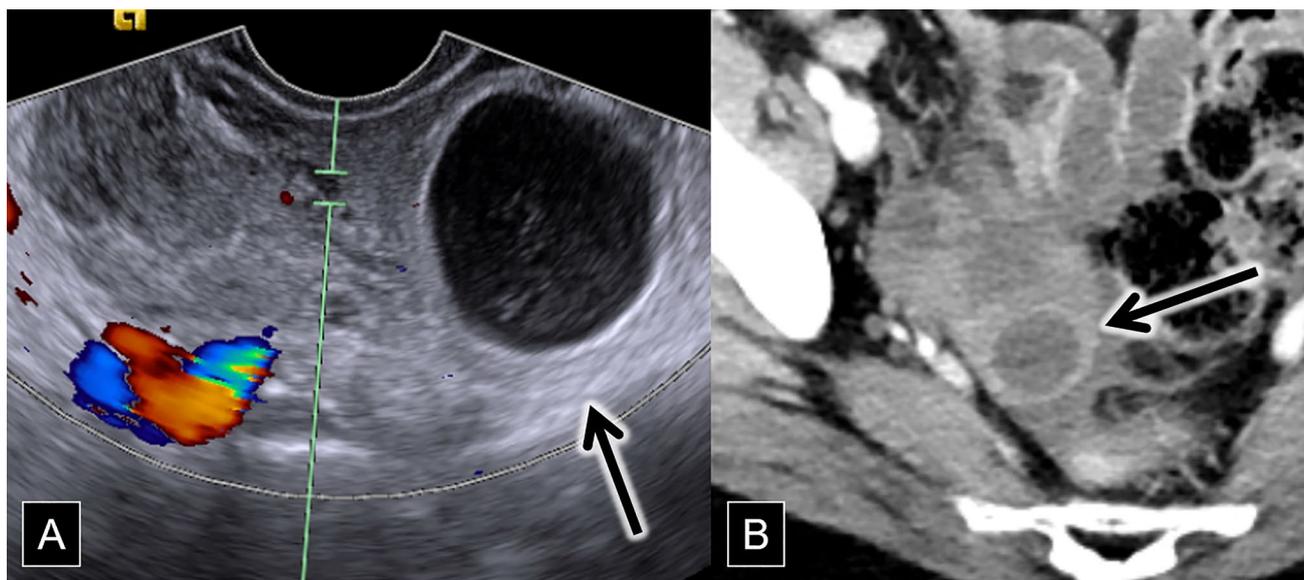
Fig. 5 32-year-old female with ovarian torsion and a corpus luteum cyst. **a** Color Doppler ultrasound image demonstrating an enlarged ovary with a corpus luteum cyst (arrow), which does not demonstrate peripheral blood flow. **b** An axial CECT image shows the enlarged ovary with adjacent free fluid, and a non-enhancing corpus luteum cyst (arrow)

CECT was superior to ultrasound for the diagnosis of CLOE in our study. Inter-reader agreement for the detection of corpus luteum peripheral hypervascularity was better on CECT compared to ultrasound, likely due to a clear difference in median (IQR) corpus luteum rim attenuation on CECT comparing CLOE to torsed ovaries with a visible corpus luteum [114.3 (103.9, 127.8) to 52.3 (50.5, 54.4) Hounsfield units; $p < 0.001$]. CECT was also more sensitive than ultrasound for detection of corpus luteum hypervascularity. Of 14 cases with peripheral hypervascularity imaged using both ultrasound and CT, 12 were demonstrated on both modalities, while 2 were only demonstrated on CT. Ultrasound excels in the morphological assessment of the ovary; specifically, it can distinguish an ovarian cyst from edematous ovarian stroma that is hypoattenuating on CT. If there is clear enhancement of a corpus luteum on CECT, then ovarian blood flow is present and additional ultrasound may not add value unless there is a question about ovarian morphology.

Torsed ovaries were significantly larger than cases of CLOE. However, the overlap in size between the two groups was such that ovarian volume may not assist in differentiating CLOE from torsion in individual cases. The largest CLOE case had an ovarian volume of 157.7 cc, which is nearly 20 times normal. The "whirlpool sign" of a twisted vascular pedicle was seen only in ovarian torsion, but was identified very infrequently.

There was a high prevalence of corpora lutea within the torsed ovaries (56.7%; 17/30), and they tended to be larger than those in cases of CLOE [median (IQR) 18.8 (8.0, 35.8) to 9.9 (5.5, 18.9) cc; $p = 0.11$]. This supports the notion a corpus luteum may act as a lead point for ovarian torsion [20, 21]. In our study, none of the corpora lutea within torsed ovaries had peripheral hypervascularity. Torsion of the right ovary (73.3%; 22/30) was more common than the left, in keeping with findings in the literature [1, 12, 22].

There are some limitations in this study. The number of cases is relatively small, as ovarian torsion without a lead-point mass is a rare diagnosis. A radiology report search tool was used to identify cases for inclusion, which could be associated with selection bias if a corpus luteum was present and the interpreting radiologist did not include it in the report. Power Doppler, which may be more sensitive for blood flow around a corpus luteum, was not routinely used during transvaginal ultrasound. The presence of peripheral vascularity of a corpus luteum may have been underestimated on ultrasound because it is operator dependent. Sensitivity for this sign may improve if more attention is paid to this prospectively. Because of the dual blood supply to the ovaries, it is theoretically possible that a corpus luteum may retain peripheral hypervascularity despite the presence of torsion, although we did not observe this in our study. Additionally, the presence of hyperemia in an edematous ovary does not exclude the possibility of intermittent torsion.

Logical avenues for further research include evaluation of corpus luteum vascularity in cases with a corpus luteum *and* a potential lead-point mass, as well as in massive ovarian edema and intermittent ovarian torsion.

Conclusion

CLOE is a benign, spontaneously resolving condition that occurs idiosyncratically after ovulation. It is associated with pelvic pain and has overlapping imaging features with ovarian torsion. The presence of peripheral hypervascularity of the corpus luteum helps distinguish CLOE from ovarian torsion, decreasing false positive diagnoses. We suggest that cases of ovarian enlargement with a clearly vascularized corpus luteum be described as "unlikely to represent ovarian torsion."

Compliance with ethical standards

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