Revista Colombiana de Obstetricia y Ginecología
ISSN: 0034-7434
ISSN: 2463-0225
Federación Colombiana de Obstetricia y Ginecología;
Revista Colombiana de Obstetricia y Ginecología

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Revista Colombiana de Obstetricia y Ginecología, vol. 69, no. 2, 2018, April-June, pp. 124-131
Federación Colombiana de Obstetricia y Ginecología; Revista Colombiana de Obstetricia y Ginecología

DOI: https://doi.org/10.18597/rcog.3042

Available in: https://www.redalyc.org/articulo.oa?id=195257686006

Revista Colombiana de Obstetricia y Ginecología Vol. 69 No. 2 • Abril-Junio 2018 • (124-131)

CASE REPORT

DOI: http://dx.doi.org/10.18597/rcog.3042

DIAGNOSIS OF APPENDICITIS IN THE THIRD TRIMESTER OF GESTATION: CASE REPORT AND REVIEW OF THE LITERATURE

Diagnóstico de apendicitis en el tercer trimestre de la gestación: reporte de caso y revisión de la literatura

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Received: July 10/17 – Accepted: May 9/18

ABSTRACT

Objective: To report the case of a woman in the third trimester of pregnancy diagnosed with perforated acute appendicitis and secondary generalised peritonitis; and to review the published literature on the usefulness of diagnostic imaging as part of the workup for this condition during the second half of pregnancy.

Materials and methods: We present the case of a 29-year-old patient, gravida 3 para 2, referred to a high complexity institution at 35.2 weeks of gestation with a diagnostic impression of pre-term labour. The patient was taken to laparotomy after remaining under observation for 20 hours of observation, with a diagnosis of abdominal pain and acute appendicitis, and was found to have perforated appendicitis with secondary peritonitis. Post-operatively, the patient developed surgical site infection and premature labour, leading to preterm delivery with satisfactory maternal and perinatal outcome. A search for articles published in English or Spanish over the past 20 years was conducted in the Up to date, Medline vía PubMed and Science Direct databases using MeSH terms "Pregnancy," "Peritonitis," "Appendicitis", "Perforated Appendicitis," "Ultrasonic Diagnosis," "Magnetic Resonance Imaging," "Computed Tomography."

Results: Overall, 20 titles directly related to the use of diagnostic imaging in pregnant women with suspected appendicitis were identified. Ultrasound is the first option used for diagnosis, but its diagnostic accuracy during the second and third trimesters is limited because, frequently, it is not possible to visualise the appendix. Sensitivity varies between 46% and 63%, and specificity between 80% and 100%. Nuclear magnetic resonance has better operational performance, with sensitivity ranging between 60% and 100%, and specificity ranging between 95% and 100%, although it is more expensive and has access limitations.

Conclusions: The diagnosis of acute appendicitis in pregnancy is challenging. Nuclear magnetic resonance would be more useful than ultrasound for diagnosis during the second and third trimesters.

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Key words: peritonitis, appendicitis, pregnancy, ultrasound diagnosis.

RESUMEN

Objetivo: reportar el caso de una paciente con embarazo avanzado de 35,2 semanas, con diagnóstico de apendicitis aguda con perforación y peritonitis generalizada secundaria, y hacer una revisión de la literatura publicada acerca de la utilidad de las imágenes diagnósticas en el análisis de esta condición en la gestante en la segunda mitad del embarazo.

Materiales y métodos: se presenta el caso de una paciente de 29 años, con 3 gestaciones, 2 partos, remitida a una institución de cuarto nivel de complejidad con gestación de 35,2 semanas e impresión diagnóstica de trabajo de parto pretérmino. Fue llevada a laparotomía luego de 20 horas de observación, con diagnóstico de dolor abdominal y apendicitis aguda; se encontró apendicitis perforada con peritonitis secundaria. En el posoperatorio presentó infección del sitio operatorio y trabajo de parto prematuro, por lo que se finalizó la gestación con evolución materna y perinatal satisfactorias. Se realizó una búsqueda con los términos MeSH: "Pregnancy", "Peritonitis", "Appendicitis", "Perforated Appendicitis", "Ultrasonic Diagnosis", "Magnetic Resonance Imaging", "Computed Tomography", en las bases de datos Up to date, Medline vía PubMed y Science Direct, para artículos publicados en inglés o español, de los últimos 20 años.

Resultados: se identificaron 20 títulos relacionados directamente con el uso de imágenes diagnósticas en mujeres gestantes con sospecha de apendicitis. El ultrasonido es la tecnología diagnóstica utilizada como primera opción, sin embargo, su desempeño diagnóstico en el segundo y tercer trimestre es limitado porque frecuentemente no se logra visualizar el apéndice. La sensibilidad varía del 46 al 63 %, y la especificidad del 80 al 100 %; la resonancia magnética tiene un mejor desempeño operativo, con una sensibilidad que varía entre el 60 y el 100 %, y una especificidad del 95 al 100 %, aunque tiene restricciones por ser más costosa y tener limitaciones de acceso.

Conclusiones: el diagnóstico de la apendicitis aguda en el embarazo es un reto diagnóstico, la resonancia magnética podría ser más útil que el ultrasonido para el diagnóstico en el segundo y tercer trimestre de embarazo.

Palabras clave: peritonitis, apendicitis, embarazo, diagnóstico ultrasonido.

INTRODUCTION

Among the causes of abdominal pain in pregnant women found in the literature, the most common is appendiceal inflammation secondary to infection or acute appendicitis (1), with a frequency of 0.4 to 1.4 for every 1000 pregnancies (2), accounting for 25% of non-obstetric surgeries during gestation (3).

Timely diagnosis is critical to avoid appendiceal perforation; however, pregnancy poses a special challenge in this condition. Although symptoms are similar as in non-pregnant women, characterised by acute abdominal pain arising from the epigastrium or the periumbilical area radiating to the right iliac fossa, usually associated with fever, vomiting and tachycardia, classical clinical signs have been described to be less precise in pregnant women. This is so due to anatomical changes such as uterine growth in the advanced stages of pregnancy, which results in displacement of the omentum, the small intestine and the abdominal wall away from the cecal appendix (4). The location of the appendix varies as gestation advances, with a cephalad displacement over McBurney's point during the first trimester, continuing through to the eighth month of pregnancy when it will be found in the right subcostal region in 80% of the cases (5). This displacement may result in delayed diagnosis and increased perforation frequency (6).

Appendiceal perforation during pregnancy has been described to be associated with higher maternal morbidity (52% vs. 17% without perforation), and mortality of up to 4% (7). On the other hand,

it has been found that acute perforated appendicitis induces increased pre-term uterine activity and pre-term delivery (8), and foetal mortality occurs in 24% when the appendix is perforated, comared with 7% when there is no perforation (9, 10) and foetal mortality occurs in 24% of cases in the presence of perforation, compared to 7% when there is no perforation (10).

As mentioned above, the diagnosis of appendicitis during pregnancy poses a challenge for obstetricians, general surgeons and general practitioners. Diagnostic tools such as Magnetic Resonance Imagine (MRI) and ultrasound are now available to help with early diagnosis, but it is important to know the quality of the evidence supporting their use in this population in order to select the best diagnostic aid. The objective of presenting this case of appendicitis during the second half of pregnancy is to review the literature on the diagnostic approach to acute appendicitis in advanced pregnancy, with emphasis on the usefulness of ultrasound and magnetic resonance imaging.

CASE PRESENTATION

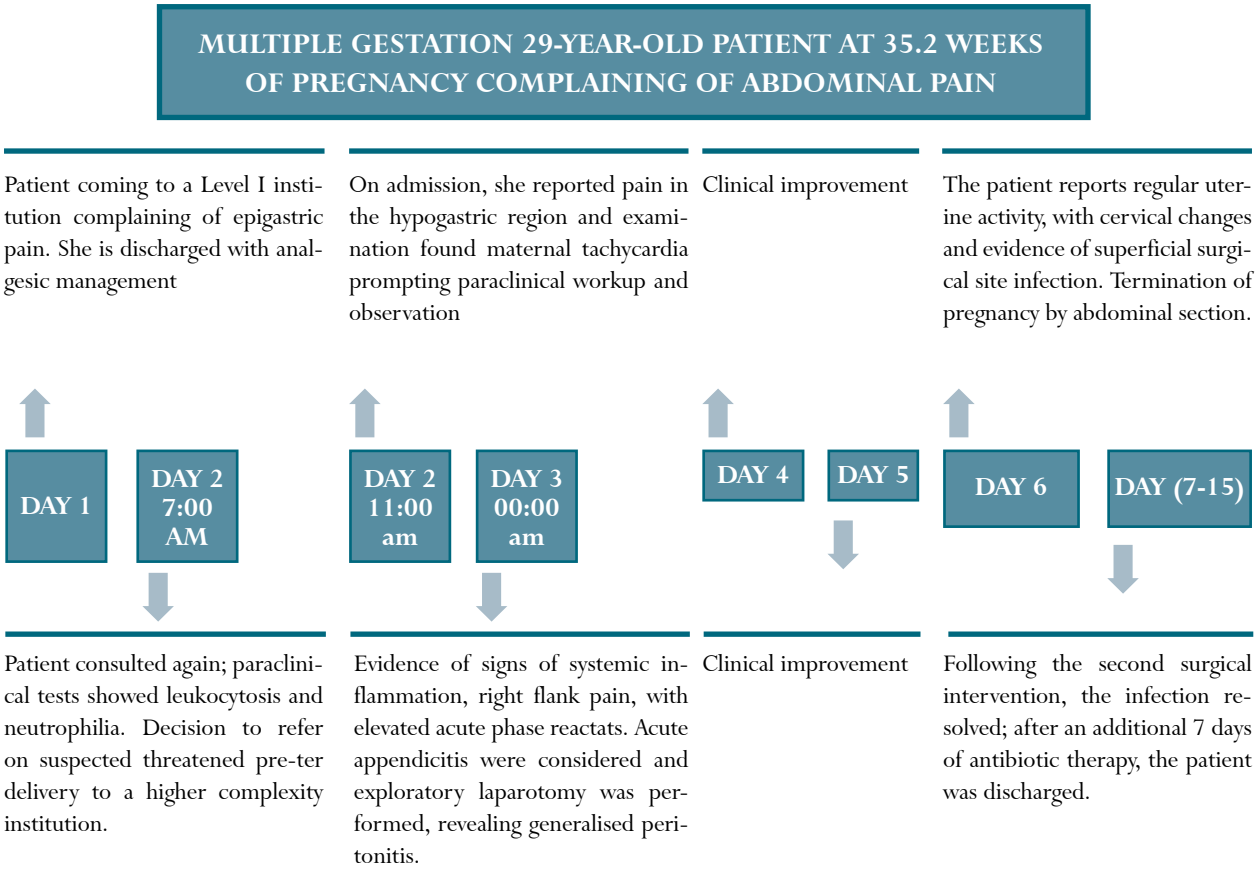
A 29-year-old, single, mestizo race pregnant woman in her 35.2 weeks of gestation based on the date of the last menstruation, was referred to a Level IV hospital in the city of Bogotá (Colombia) from a primary care institution due to a 24-hour clinical picture characterised by epigastric pain which did not respond to the administration of a histamine receptor antagonist. Whole blood count showed leukocytosis and neutrophilia, while urinalysis results were normal. Impending pre-term delivery was considered, prompting the decision to refer the patient (Figure 1). On admission, the patient reported pain in the hypogastric region with no other associated symptoms; the only significant medical history. Obstetric history included two prior uncomplicated pregnancies. Current pregnancy was negative for STORCH (syphilis, toxoplasma, rubella, cytomegalovirus, herpes, hepatitis B), first and second trimester ultrasound scans consistent with the gestational age, the only relevant information being primipaternity.

The initial physical examination found the following values: blood pressure 115/66 mm/Hg, heart rate 97 beats per minute, respiratory rate 18 breaths per minute, temperature 36.5°C, arterial oxygen saturation 95%, as well as pain on palpation over the lower hemiabdomen and evidence of irregular uterine activity. Ligamentous distension was considered and the patient was placed under observation. Whole blood count showed a result of 15,900 leukocytes/mm3), at the expense of neutrophils, elevated CRP (C-reactive protein), normal liver function, and urinalysis not indicative of infection. After a period of 20 hours, the patient showed clinical signs of systemic inflammatory response with a febrile peak and tachycardia, right flank pain and voluntary abdominal defense. Foetal monitoring showed foetal tachycardia, attributed to maternal fever. Follow-up laboratory tests showed elevated acute phase reactants with persistent CRP elevation and increased leukocytosis.

Because of suspected appendicitis the patient was assessed by the general surgery service and exploratory median laparotomy was performed given the possibility of abdominal surgical pathology, with the finding of acute, middle-third perforated appendicitis in gangrenous phase and generalised peritonitis. Appendectomy plus peritoneal lavage were performed, and antibiotic treatment with piperacillin/tazobactam 4.5 mg IV every 6 hours plus metronidazole 500 mg IV every 8 hours was initiated.

Post-operatively there was evidence of increased surgical site erythema and, additionally, the patient reported uterine activity. The gynaecological examination revealed cervical changes, 3 cm dilation with 70% effacement, and foetal monitoring with irregular uterine activity. Reassessment by general surgery found superficial complicated surgical site infection and reintervention was indicated for open

Figure 1.
Timeline of the patient's condition during hospital stay



Source: Authors.

surgical wound management; during the procedure, evidence was found of fascial dehiscense, prompting intra-operative assessment by the ObGyn service. Based on the finding of active infection in the abdominal cavity and the risk of maternal sepsis with foetal compromise, it was decided to deliver the foetus during the same surgical time by means of a cesarean section. Both procedures were carried out uneventfully with the result of a live newborn weighing 3340 g, and measuring 48 cm, with a low APGAR score that recovered later. The mother and the baby remained in the hospital until the completion of a 7-day course of antibiotics.

MATERIALS AND METHODS

A search was conducted in the literature in Up to date, Medline via PubMed and Science Direct databases using the MeSH terms "Pregnancy", "Peritonitis", "Appendicitis", "Perforated Appendicitis", "Ultrasonic Diagnosis", "Magnetic Resonance Imaging" and "Computed Tomography". The search included case reports, review of the literature, descriptive retrospective studies, cohorts, and case-control studies published in English or Spanish over the past 20 years focusing on the topic of appendicitis in advanced pregnancy, and those that dealt with the approach to diagnosis. Letters to the editor were excluded.

Ethical considerations. The patient signed the informed consent and gave permission for her case to be published. Information confidentiality and patient privacy were guaranteed.

RESULTS

Overall, 10 titles pertaining to the use of imaging for diagnosis of appendicitis during pregnancy were identified. They included three retrospective cohort studies (11-13), five cross-sectional studies (14-18), one prospective cohort (19), and one review of the literatura (20). The studies had been conducted in the United States (12-15), Canada (17, 18), Brazil (20), Turkey (11), Iran (19), and South Korea (16).

Ultrasound. In their review of the literature, Franca et al. argue that the diagnostic approach to appendicitis during its initial stages is challenging in pregnant women, particularly during the second and third trimesters. Moreover, they indicate that the first diagnostic test should be ultrasound, and recommend nuclear magnetic resonance when ultrasound results are inconclusive, and they propose the use of computed axial tomography (CT) as a last resort (20).

In a retrospective cohort of pregnant and non-pregnant women taken to appendectomy, Aras et al. report that sensitivity and specificity of ultrasound for the diagnosis of appendicitis in a pregnant woman are 61% and 80%, respectively. They suggest a careful assessment in patients with suspected appendicitis in whom ultrasound is reported as inconclusive or normal because, in women in the third trimester of pregnancy, pain may be localised to the right upper quadrant and there is usually a slight leukocyte elevation during this stage of gestation, creating a diagnostic limitation (11).

In a prospective cohort study, Kazemini *et al.* assessed the accuracy of ultrasonography in the diagnosis of acute appendicitis in pregnancy. They studied 58 pregnant women with a mean age of 29.1 years ± 4.94 diagnosed with acute appendicitis histologically confirmed, between January 2014 and January 2016. They report that the greater the gestational age the lower the sensitivity but the higher the specificity, and they report a sensitivity of 63% in the second trimester and 50% in the third trimester, and a specificity of 75% and 100%, respectively, with a positive odds ratio of 2.52 and a negative odds ratio of 0.49 for the second trimester. These authors recommend the use of other imaging studies such as computed tomography or magnetic resonance following an inconclusive ultrasound result (19).

Shetty *et al.* conducted a retrospective cross-sectional study of clinical records over a 5-year period, focusing on diagnostic imaging in patients with clinical suspicion of appendicitis; they correlated imaging findings with patient management and final outcome. A total of 39 patients were referred for diagnostic imaging studies; of them, 35 were assessed with ultrasound and 23 of them were later taken to computed axial tomography, while 4 were taken to CT scan directly without having an ultrasound first. These authors conclude that the method most widely used for diagnosis is ultrasound, with 46.1% sensitivity and 95.4% specificity. Low specificity could be explained because it is often impossible to visualise the appendix (14).

Magnetic resonance imaging. In a retrospective study, Theilen et al. assessed the accuracy of magnetic resonance imaging in the diagnosis of appendicitis in 171 pregnant women suspected of having this condition. They report that it was not possible to visualise the appendix in 53, but none of them had appendicitis in the end. Of those patients in whom the diagnosis was a normal appendix, only 1 had appendicitis, and in 18 with a diagnosis of abnormal appendix, 6 had false positive results. Consequently, sensitivity and specificity of NMR were 91% and 95.3%, respectively. The authors also mention that the more advanced the pregnancy is, the lower the rate of visualisation but that, none-

theless, it is better than ultrasound, which did not allow visualisation in 43 out of 46 pregnant women in whom it was performed. Of the three women in whom visualisation was possible, an abnormal appendix was diagnosed in 2 and confirmed only in 1 as well as in the patient considered to have a normal appendix. Of the 43 patients in whom the appendix was not visualised, the diagnosis was made later in 28 using NMR (12).

Israel *et al*., conducted a retrospective cohort study with 33 patients with suspected appendicitis. In 5 patients, appendicitis was confirmed; NMR identified an abnormal appendix in the 4 cases of acute appendicitis; in 13, a normal appendix was diagnosed; in no cases was the diagnosis of appendicitis found in the clinical record; and in 16 cases it was not possible to identify the appendix and one of those cases resulted in chronic appendicitis. Consequently, sensitivity was 80% and specificity was 100%. These authors reported that the appendix could not be identified with ultrasound in 29 patients, a normal appendix was reported in 3 cases, 1 of which was diagnosed as having acute appendicitis in the end. These authors do not report the gestational age at which imaging studies were performed (13).

Tsai *et al.* conducted a retrospective cross-sectional study aimed at determining the degree of inter-radiologist agreement regarding the features of magnetic resonance imaging of the appendix during pregnancy, together with the results associated with an indeterminate interpretation. They studied 233 women with suspected appendicitis during pregnancy between 2003 and 2015, taken to magnetic resonance imaging during that period. Overall, there were 14 patients (6%) positive for acute appendicitis during pregnancy; in 13 of them, NMR was interpreted as abnormal and in 1 patient, it was interpreted as normal. The kappa value for inter-observer agreement was 0.85 - 1; appendicitis was not the final outcome in 73 patients in whom the appendix was not visualised (15).

Jung *et al.* conducted a retrospective cross-sectional study to assess the diagnostic accuracy of NMR in appendicitis. The study included 46 pregnant women who were taken to magnetic resonance imaging because of suspected acute appendicitis, between 2010 and 2016; NMR was shown to have 100% sensitivity and 91% specificity; this imaging modality allowed to categorise appendicitis as probable appendicitis alone, appendicitis associated with another pelvic pathology, and definitive diagnosis of appendicitis. Two of the three cases of false positive results with NMR occurred with the probable diagnosis of appendicitis associated with another pathology (16).

In another retrospective cross-sectional study in 42 pregnant patients with suspected appendicitis taken first to ultrasound and then to magnetic resonance between August 2008 and 2015, Patel *et al*. set out to determine the diagnostic accuracy of the 42 magnetic resonance imaging studies. Overall, 5 patients were diagnosed with acute appendicitis, and 7 appendectomies were performed. Ultrasound did not identify the appendix in any of the patients, whereas it was identified in 22 patients when NMR was used, classifying 6 cases as appendicitis and 16 as normal appendices. There were 20 cases in which the appendix was not visualised and in none of them was appendicitis diagnosed within the next 6 months. Finally, using nuclear magnetic resonance, 3 cases of acute appendicitis were adequately identified, 3 cases were considered false positive, and in 36 appendices classified as normal, 34 were true negative and 2 were false positive, for 60% sensitivity and 92% specificity (17).

Burns *et al*., in a retrospective cross-sectional study, assessed the performance of NMR for the diagnosis of appendicitis during pregnancy in a Canadian institution. The authors reviewed all magnetic resonance images performed between 2006 and 2012 in order to assess pregnant women for suspected appendicitis. A total of 71 magnetic resonance images were reviewed and the appendix

was identified in 40 patients (56.3%), for 75% sensitivity and 100% specificity of NMR for the diagnosis of appendicitis in pregnant women (18).

CONCLUSIONS

Diagnosing appendicitis during pregnancy is challenging, in particular during the second and third trimesters, because of the cephalad displacement of the appendix. Despite the fact that ultrasound is considered the first choice because of ease and low cost, its sensitivity ranges between 46% and 63%, while its specificity ranges between 85% and 100%. Sensitivity diminishes as gestational age increases, when the appendix is seldom identified. Nuclear magnetic resonance is more expensive and less readily available, and has a sensitivity ranging between 60% and 100%, and a specificity of 91% to 100%. This diagnostic modality would be more useful during the second and the third trimesters of gestation. In the studies included in this review, there were no cases of appendicitis when the appendix was not visualised.

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Conflict of interest: none declared.