
Dennis A Bloomfield, FACC, FACP, FRACP, FRCP (Hon), MD, MRCP,
Professor

Editor-in-Chief

World Journal of Clinical Cases

JAN 1, 2021

Dear Dr. Bloomfield,

We thank the reviewers for pointing out the issues and agree with the reviewers. We have revised the manuscript, based on the helpful critique from the reviewers. We make a point-to-point response to the issues as follows. The revised parts are underlined for easy identification.

Issues and responses

Reviewer #1:

1. **Issue:** The most center will still diagnose EPN by CT scan. We think this sign is not so specific for EPN. It might be difficult to differentiate EPN from duodenal or colonic perforation, and many other possibilities. How do the authors explain about this?

Response : Thanks a lot for the helpful comments. We agree with the reviewer that most centers diagnose EPN by CT scan which is accurate and remains the gold standard for diagnosing EPN^[1]. But CT scan is time-consuming, risky due to radiation exposure and unavailable for some very critical patients, such as patients with severe hypotension. POCUS is portable, noninvasive, and immediate, and provides real-time information at the bedside without radiation, challenging CT scan especially in emergency and critical care medicine^[2]. Studies have shown that POCUS promotes a timely initial diagnosis in EPN in emergency rooms^[3,4]. However, further CT scan is still needed to confirm the diagnosis and to assess the site and size of EPN. We suggest that both CT scan and POCUS complement each other in diagnosis of EPN.

We agree with the reviewer that the “falls” sign was not an absolute marker in the diagnosis of EPN. Intraperitoneal hollow organ perforation usually results in free gas in peritoneal cavity. However, rare extraperitoneal hollow organ perforation, such as perforation of the descending duodenum, and necrotic pancreatitis may lead to free gas in retroperitoneum, such as perirenal space^[5-7]. Thus, gas in perirenal space detected by POCUS should be differentiated between EPN and extraperitoneal hollow organ perforation or necrotic pancreatitis. As our case showed, the patient had a soft abdomen without symptoms of enteroparalysis and further CT scan showed signs of upper urinary tract infection, such as an enlarged kidney and perirenal fat stranding. The duodenal perforation and necrotic pancreatitis were unlikely the causes of the perirenal gas. Though confirmed diagnosis of EPN relies on CT scan and clinical manifestations, POCUS facilitates the initial diagnosis rapidly and promotes early and aggressive care which reduces the high mortality resulting from diagnostic delays.

We agree with the reviewer that gas in the perirenal space on POCUS should be differentiated from other possibilities. Gas and stones always mimic each other on ultrasound^[8]. As such, perirenal gas should be differentiated from perirenal calcification or renal wall calcification. Perirenal calcification and renal wall calcification are non-specific pathologies in perirenal tumors^[9], renal wall tuberculosis^[10], polycystic kidney disease^[11] and other very rare diseases such as Erdheim-Chester disease^[12] and tumoural calcinosis^[13]. Calcification usually presents with clean shadowing on POCUS, but gas usually presents with dirty shadowing^[14]. We suggest that physicians can differentiate perirenal calcification and gas by POCUS on the basis of accurate knowledge of ultrasound and adequate faculty training.

As we know, the case report might be in the tail of the hierarchy of evidence-based medicine, but it can describe important scientific

observations that are missed or undetected in clinical trials^[15]. We think the essence of our case report is not only to report a new sign, but also to highlight the importance of air-related imaging features on POCUS in diagnosis of EPN. Given the limitation of the case report, we suggest further cohort clinical studies are needed to assess the diagnostic accuracy of air-related artifacts on POCUS versus CT for diagnosis of EPN. We have revised the manuscript according to the comments.

Revision:

1. Although CT is the gold standard for diagnosing EPN^[1,16], POCUS is portable and provides real-time information at the bedside without radiation exposure, and has become a promising tool facilitating rapid diagnosis in the past two decades^[2]. (Discussion: Paragraph 5)
2. Gas in the right perirenal space may result from necrotic pancreatitis and extraperitoneal hollow organ perforation, such as perforation of the descending duodenum^[6,7]. The patient had a soft abdomen without symptoms of enteroparalysis and further CT scan showed upper urinary tract infection. Hence, duodenal perforation and necrotic pancreatitis were unlikely to be the causes of gas in the right perirenal space. (Final diagnosis)
3. The “falls” sign should be differentiated between perirenal gas and perirenal calcification or renal wall calcification which is non-specific pathology in renal wall tuberculosis^[10], perirenal tumors, polycystic kidney disease and very rare diseases such as Erdheim-Chester disease and tumoural calcinosis^[9,11-13]. In most cases, perirenal calcification and urinary stones present with clean shadowing which is an absolute anechoic band. (Discussion: Paragraph 7)
4. Given the limitation of the case report, further cohort studies are needed to assess the diagnostic accuracy of air-related artifacts on POCUS versus CT imaging for EPN. (Discussion: Paragraph 7)

Reviewer #2: None.

Reviewer #3:

1. **Issue:** How to standardize the reliability of the air-related sonograph with POCUS?

Response: Thanks a lot for this constructive comment. We have revised the part showing how to standardize the reliability of the air-related artifacts on POCUS in EPN.

Revision: But physicians should keep in mind that these air-related artifacts on POCUS vary in different cases. The variation not only results from multiple effects of gas bubbles such as volume, shape, position, and orientation, but also correlates with a mismatch of acoustic impedance between the gas bubbles and its surrounding renal tissues^[17]. Moreover, the utility of POCUS remains a challenge as a result of its dependence on the skills and experience of the operators, especially nonimaging professionals^[2]. So, we suggest that the standardization of the air-related artifacts on POCUS in EPN should be implemented on the basis of sufficient faculty training. (Discussion: Paragraph 5)

2. **Issue:** What are the suggestions for the future research regarding the comet tail artifacts and the "fall" sign so the next authors could replicate the study to test the hypothesis. For instance, the clinical research to address the value of new medical tests.

Response: We have revised the part providing the suggestion for the future research regarding the comet-tail artifacts and the "falls" sign.

Revision: Given the limitation of the case report, further cohort studies are needed to assess the diagnostic accuracy of air-related artifacts on POCUS versus CT imaging for EPN. (Discussion: Paragraph 7)

Reviewer #4: None.

We appreciate very much your kind consideration for publication of our manuscript and look forward to hearing from you at your earliest convenience.

Yours sincerely,

Dr. Zhou-Xiong Xing

Department of Critical Care Medicine, Affiliated Hospital of Zunyi Medical University, Zunyi 563000, Guizhou Province, China

REFERENCES

- 1 Elawdy MM, Osman Y, Abouelkheir RT, El-Halwagy S, Awad B, El-Mekresh M. Emphysematous pyelonephritis treatment strategies in correlation to the CT classification: have the current experience and prognosis changed. *Int Urol Nephrol* 2019; **51**: 1709-1713 [PMID: 31309391 DOI: 10.1007/s11255-019-02220-3]
- 2 Bhagra A, Tierney DM, Sekiguchi H, Soni NJ. Point-of-Care Ultrasonography for Primary Care Physicians and General Internists. *Mayo Clin Proc* 2016; **91**: 1811-1827 [PMID: 27825617 DOI: 10.1016/j.mayocp.2016.08.023]
- 3 McCafferty G, Shorette A, Singh S, Budhram G. Emphysematous Pyelonephritis: Bedside Ultrasound Diagnosis in the Emergency Department. *Clin Pract Cases Emerg Med* 2017; **1**: 92-94 [PMID: 29849419 DOI: 10.5811/cpcem.2016.12.32714]
- 4 Brown N, Petersen P, Kinas D, Newberry M. Emphysematous Pyelonephritis Presenting as Pneumaturia and the Use of Point-of-Care Ultrasound in the Emergency Department. *Case Rep Emerg Med* 2019; **2019**: 6903193 [PMID: 31565445 DOI: 10.1155/2019/6903193]
- 5 Sakurai Y, Miura H, Matsubara T, Imazu H, Hasegawa S, Ochiai M. Perforated duodenal diverticulum successfully diagnosed preoperatively with abdominal CT scan associated with upper gastrointestinal series. *J Gastroenterol* 2004; **39**: 379-383 [PMID: 15168251 DOI: 10.1007/s00535-003-1306-5]
- 6 Mehdi S, Singh V, Sinha RJ, Pandey S. Concealed diagnosis of duodenal perforation in a patient with emphysematous pyelonephritis: the dilemma of air in the right perirenal space. *BMJ Case Rep* 2019; **12** [PMID: 30765455 DOI: 10.1136/bcr-2018-228629]
- 7 Han SY, Tishler JM, Aldrete JS. Extraperitoneal gas: compartmental localization and identification of source. *J Can Assoc Radiol* 1985; **36**: 17-21 [PMID: 3980549]
- 8 Koratala A, Bejjanki H. Point-of-care ultrasound for the nephrologist: emphysematous pyelonephritis versus staghorn calculus. *Clin Exp Nephrol* 2019; **23**: 1257-1258 [PMID: 31267261 DOI: 10.1007/s10157-019-01763-0]
- 9 Yoshino T, Sejima C, Oka Y, Taniguchi H, Nagami T, Wake K, Yamamoto T, Ohnuma H, Kodama K, Kanazawa A, Kawakami K. [Retroperitoneal Dedifferentiated Liposarcoma with Metaplastic Bone Formation : A Case Report and Review of the Literature]. *Hinyokika Kyo* 2019; **65**: 151-155 [PMID:

-
- 31247692 DOI: 10.14989/ActaUrolJap_65_5_151]
- 10 Lu P, Li C, Zhou X. [Significance of the CT scan in renal tuberculosis]. *Zhonghua Jie He He Hu Xi Za Zhi* 2001; **24**: 407-409 [PMID: 11802996]
 - 11 Levine E, Grantham JJ. Calcified renal stones and cyst calcifications in autosomal dominant polycystic kidney disease: clinical and CT study in 84 patients. *AJR Am J Roentgenol* 1992; **159**: 77-81 [PMID: 1609726 DOI: 10.2214/ajr.159.1.1609726]
 - 12 Villatoro-Villar M, Koster MJ. Erdheim-Chester Disease with atrial mass and perinephric calcification. *Clin Case Rep* 2017; **5**: 2153-2154 [PMID: 29225878 DOI: 10.1002/ccr3.1258]
 - 13 Xia M, Liu C, Yang H, Yin K, Wang Y, Tong X, Zhang S, Shuang W. A case report: renal cystic tumoural calcinosis with ossification and bone marrow formation. *BMC Urol* 2020; **20**: 106 [PMID: 32689989 DOI: 10.1186/s12894-020-00675-6]
 - 14 Rubin JM, Adler RS, Bude RO, Fowlkes JB, Carson PL. Clean and dirty shadowing at US: a reappraisal. *Radiology* 1991; **181**: 231-236 [PMID: 1887037 DOI: 10.1148/radiology.181.1.1887037]
 - 15 Alsaywid BS, Abdulhaq NM. Guideline on writing a case report. *Urol Ann* 2019; **11**: 126-131 [PMID: 31040594 DOI: 10.4103/UA.UA_177_18]
 - 16 Tasleem AM, Murray P, Anjum F, Sriprasad S. CT imaging is invaluable in diagnosing emphysematous pyelonephritis (EPN): a rare urological emergency. *BMJ Case Rep* 2014; **2014** [PMID: 24706709 DOI: 10.1136/bcr-2014-204040]
 - 17 Buttar S, Cooper D Jr, Olivieri P, Barca M, Drake AB, Ku M, Rose G, Siadecki SD, Saul T. Air and its Sonographic Appearance: Understanding the Artifacts. *J Emerg Med* 2017; **53**: 241-247 [PMID: 28372830 DOI: 10.1016/j.jemermed.2017.01.054]