ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2018 December 26; 6(16): 1073-1222

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

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INDEXING/ABSTRACTING

World Journal of Clinical Cases (*WJCC*) is now indexed in PubMed, PubMed Central, Science Citation Index Expanded (also known as SciSearch®), and Journal Citation Reports/Science Edition. The 2018 Edition of Journal Citation Reports cites the 2017 impact factor for WJCC as 1.931 (5-year impact factor: N/A), ranking WJCC as 60 among 154 journals in Medicine, General and Internal (quartile in category Q2).

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Semimonthly

EDITORIAL OFFICE
Jin-Lei Wang, Director

World Journal of Clinical Cases
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7901 Stoneridge Drive,
Suite 501, Pleasanton, CA 94588, USA
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Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
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PUBLICATION DATE
December 26, 2018

INSTRUCTIONS TO AUTHORS
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World J Clin Cases 2018 December 26; 6(16): 1175-1181

DOI: 10.12998/wjcc.v6.i16.1175

ISSN 2307-8960 (online)

CASE REPORT

Post-appendectomy pelvic abscess with extended-spectrum beta-lactamase producing *Escherichia coli*: A case report and review of literature

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Author contributions: Tse A and Cheluvappa R performed research and wrote this paper; Cheluvappa R addressed reviewers' comments and did the final submission; Selvendran S designed research and supervised the writing of this paper.

Informed consent statement: Informed consent was obtained from the patient, and appropriate signed documentation was obtained and retained.

Conflict-of-interest statement: The authors have no conflicts of interests to declare.

CARE Checklist (2013) statement: Guidelines of the CARE Checklist (2013) have been adopted while writing this manuscript.

Manuscript source: Invited manuscript

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Received: October 19, 2018
Peer-review started: October 19, 2018
First decision: November 12, 2018
Revised: November 11, 2018
Accepted: November 14, 2018
Article in press: November 15, 2018
Published online: December 26, 2018

Abstract

BACKGROUND

Appendicitis, the inflammation of the appendix, is the most common abdominal surgical emergency requiring expedient surgical intervention. Extended-spectrum beta-lactamases (ESBLs) are bacterial enzymes that catalyse the degradation of the beta-lactam ring of penicillins and cephalosporins (but without carbapenemase activity), leading to resistance of these bacteria to beta-lactam antibiotics. Recent increases in incidence of ESBL-producing bacteria have caused alarm worldwide. Proportion estimates of ESBL-Enterobacteriaceae hover around 46% in China, 42% in East Africa, 12% in Germany, and 8% in the United States.

CASE SUMMARY

The impact of ESBL-producing bacteria on appendiceal abscesses and consequent pelvic abscesses are yet to be examined in depth. A literature review using the search words "appendiceal abscesses" and "ESBL *Escherichia coli* (*E. coli*)" revealed very few cases involving ESBL *E. coli* in any capacity in the context of appendiceal abscesses. This report describes the clinical aspects of a patient with appendicitis who

developed a postoperative pelvic abscess infected with ESBL-producing *E. coli*. In this report, we discuss the risk factors for contracting ESBL *E. coli* infection in appendicitis and post-appendectomy pelvis abscesses. We also discuss our management approach for post-appendectomy ESBL *E. coli* pelvic abscesses, including drainage, pathogen identification, and pathogen characterisation. When ESBL *E. coli* is confirmed, carbapenem antibiotics should be promptly administered, as was done efficaciously with this patient. Our report is the first one in a developed country involving ESBL *E. coli* related surgical complications in association with a routine laparoscopic appendectomy.

CONCLUSION

Our report is the first involving ESBL *E. coli* and appendiceal abscesses, and that too consequent to laparoscopic appendectomy.

Key words: Appendectomy; Appendiceal abscess; Appendicitis; Beta-Lactam; Antibiotic resistance; Beta-Lactamase; Carbanepem; Cephalosporin; *Escherichia coli*; Extended-spectrum beta-lactamase; Infection; Pelvic abscess; Penicillin; Case report

Core tip: This report describes the clinical aspects of a patient with appendicitis who developed a postoperative pelvic abscess infected with extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* (*E. coli*). Our report is the first reliable report involving ESBL *E. coli* and appendiceal abscesses. This report is also the first one in a developed country involving ESBL *E. coli* related surgical complications in association with a routine laparoscopic appendectomy.

Tse A, Cheluvappa R, Selvendran S. Post-appendectomy pelvic abscess with extended-spectrum beta-lactamase producing *Escherichia coli*: A case report and review of literature. *World J Clin Cases* 2018; 6(16): 1175-1181
URL: https://www.wjgnet.com/2307-8960/full/v6/i16/1175.htm
DOI: https://dx.doi.org/10.12998/wjcc.v6.i16.1175

INTRODUCTION

Extended-spectrum beta-lactamases (ESBLs) are bacterial enzymes that lead to the degradation of the beta-lactam ring of penicillins, cephalosporins, and monobactams (but not carbapenems) leading to these beta-lactam antibiotics being ineffective in treating infections with bacteria producing ESBLs[1]. Beta-lactamase inhibitors, such as clavulanic acid, inhibit ESBLs. However, there is sparse evidence available for good clinical outcomes with beta-lactamase inhibitor combinations[2]. The bacterial ESBLs are commonly encoded by transferable multi-antibiotic resistance plasmids, often including resistance to aminoglycosides[2]. Therefore, the antibiotic choices are limited to carbapenems (drug-group of choice), fluoroquinolones, tigecycline and polymyxins[2]. The substantial increases in recent worldwide prevalence of ESBL-producing bacteria have alarmed public health officials and infectious diseases personnel[1]. Bacteria producing ESBLs have been isolated with significant rates in Asia, Latin America and the Middle East[3]. Recent global increases in faecal colonisation by ESBL bacteria have been noted[4]. South and South East Asia are considered to be major regions for ESBL related infections and colonisation[5-7]. A Pakistani meta-analysis estimated the proportion of ESBL Enterobacteriaceae colonisation (nosocomial and community) to be 40%[8]. Proportion estimates of ESBL Enterobacteriaceae hover around 46% in China[9], 42% in East Africa[10], 10% to 15% in Germany[11], and 4% to 12% in the United States[12,13]. These data have significant clinical and public health import. However, the specific impact of ESBL bacteria on appendiceal abscesses and consequent pelvic abscesses are yet to be determined.

The human vermiform appendix has abundant lymphoid tissue and is exposed constantly to gastrointestinal bacteria and viruses of various hues. Inflammation of the appendix is termed "appendicitis". The causality of acute appendicitis has been shrouded in mystery, although the most popular theory posits luminal obstruction of the appendix (by faecoliths, lymphoid hyperplasia, or malignancy) incarcerating gut secretions, leading to increased intraluminal pressure and mucosal ischemia, resulting in gut bacterial infection[14]. The incidence of appendicitis is approximately 7%, making it the most common abdominal pathology requiring emergency surgery[15]. The peak incidence of appendicitis without perforation is in the 2nd and 3rd decades of life[16]. Mortality due to acute appendicitis is around 0.3%[17]. The mortality increases to 1.7% if perforation is present[17]. The approximate annual incidence of acute appendicitis in Australia is 177 per 100000[18]. Appendectomy for appendicitis is one of the most common emergency surgeries performed in public hospitals in Australia[19]. A well-known complication of appendectomies is the development of postoperative intra-abdominal abscesses. It occurs in 3% to 25% of appendectomies[20,21], with higher occurrences after perforated or gangrenous appendicitis[22-25].

Our patient was a 16-year-old girl from a Pakistani background who presented with acute appendicitis but went on to develop a pelvic abscess with ESBL *E. coli* after laparoscopic appendectomy. We monitored and treated this patient at various stages. Data was collated from progress notes, procedure summaries, pathology reports, radiology films or reports, surgical procedure-entries, and clinical files pertaining to this patient. We carried out a systematic literature search on Pubmed and Google Scholar using different combinations of the words: appendiceal, appendicitis,

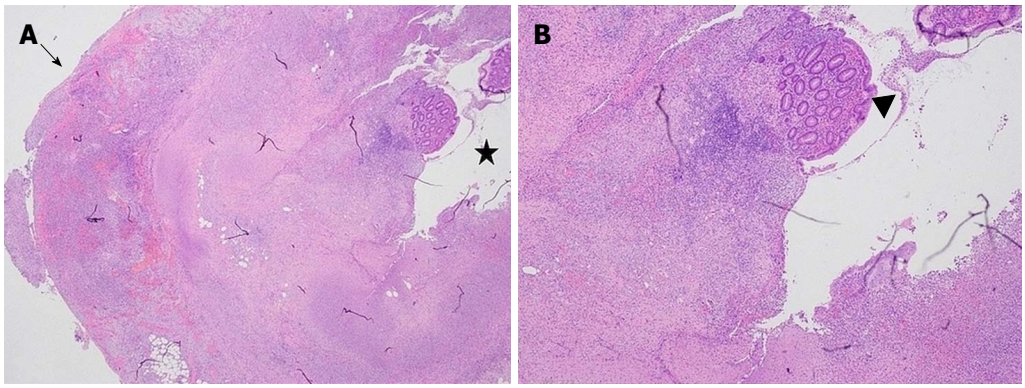

Figure 1 Histopathology of appendiceal specimen with appendicitis. A: This slide is a cross-section of the appendix showing the appendiceal lumen indicated by the star displaying extensive ulceration and pervasive inflammation; with minimal residual mucosa. The transmural inflammation, involves the serosa as shown by the arrow; and depicts mucosal ulceration and necrosis; B: This slide image, photographed at a higher magnification, shows the residual mucosa (which appears normal) surrounded by necrotic tissue and cellular debris. The residual mucosa is indicated by the arrowhead.

appendectomy, appendicectomy, abscess, ESBL, extended spectrum beta lactamase, or *E. coli*. There have only been 2 previous reports involving ESBL *E. coli* in any context of appendiceal abscesses. One of the 2 reports was 6-years-old, and the other, 9-years-old[26,27]. Unfortunately, those 2 reports appeared to be from publications not affiliated to reputable publishing houses[26,27]. Moreover, those 2 reports are not indexed in PubMed[26,27].

CASE PRESENTATION

A 16-year-old girl of Pakistani extraction presented with a 7-d-history of right iliac fossa pain with anorexia, diarrhoea, and a body temperature of 38.7 ℃. Her outpatient ultrasound scan did not show the appendix, although the possibility of the presence of a right ovarian cyst was suspected. Laboratory examination showed elevated levels of inflammatory markers: white cell count (WCC) 21.61 x 10^9/L, and C reactive protein (CRP) 69 mg/L. Based on these findings, a clinical diagnosis of appendicitis was made and the patient was commenced on 1 g Ceftriaxone daily and 500 mg of Metronidazole twice-daily. The patient underwent emergency surgery on the same night of arrival. On laparoscopy, a large phlegmon was identified, encompassing a perforated appendix and a faecolith. An appendectomy was performed with irrigation of the right para-colic gutter and pelvis with approximately 500 mL of normal saline, which we thought was adequate. The appendiceal stump area chosen for closure with Polydioxanone Endoloop® was free from visible inflammation. A 15 French Blake drain was placed in the pelvis extending to the right iliac fossa at the site of the phlegmon.

Subsequent histopathological examination reported acute suppurative and necrotic appendix (Figure 1). The 15 French Blake drain was removed on post-operative day 2 with minimal drainage. However, on postoperative day 3**,** the patient developed persistent pyrexia of 38.2 ℃, in conjunction with increased haematological inflammatory markers (WCC 28.78 x 10^9/L, CRP 100 mg/L). A computed tomography (CT) scan performed on day 4 showed a large pelvic collection 10.1 cm x 9.6 cm (Figures 2 and 3).

FINAL DIAGNOSIS

The CT report stated that there was "a peripheral enhancing collection in the pelvis on the right tracking inferiorly and along anterior pelvic side wall, crossing the midline, and being continuous with a large low density collection containing high density material in the pouch of Douglas".

TREATMENT

The pelvic collection in the pouch of Douglas was drained percutaneously under CT-guidance, and an 8 French Pigtail drain was left *in situ* in the rectouterine pouch of Douglas (Figure 4).

The tissue culture and percutaneously drained collection culture grew ESBL *E. coli*, susceptible only to Gentamicin and Meropenem. Our patient's antibiotic regimen was then changed from Ceftriaxone and Metronidazole to Meropenem. Meropenem was given for 5 d during the patient's hospital stay. On postoperative day 9, the percutaneous 8 French Pigtail drain was removed under aseptic conditions and the patient was discharged.

MULTIDISCIPLINARY EXPERT CONSULTATION

Under the instructions of the Infectious Diseases Specialist, a further 4 d of Irtepenum were given to the patient to be taken as an outpatient in ambulatory care.

OUTCOME AND FOLLOW-UP

Follow up ultrasounds were done at discharge and 2

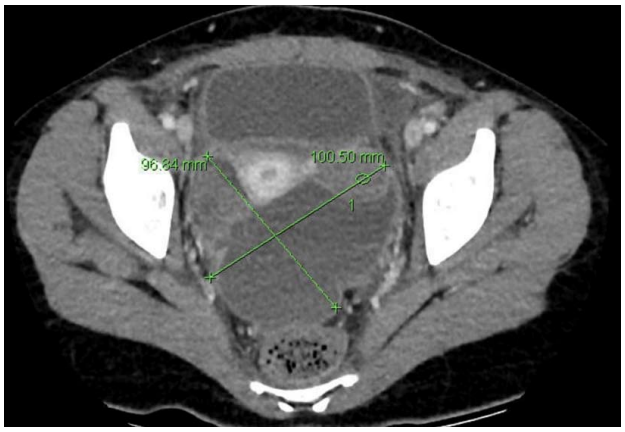

Figure 2 Pelvic collection - axial view. The computerised tomography (CT) scan on postoperative day 4 shows a large pelvic collection with dimensions of 10.1 cm × 9.6 cm. This CT view is the axial view. The collection shows different segments displaying different densities.

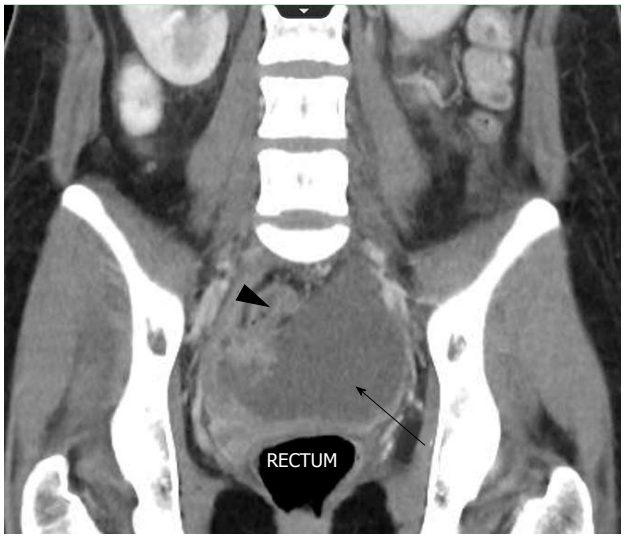

Figure 3 Pelvic collection - coronal view. The computerised tomography (CT) scan on postoperative day 4 shows a large pelvic collection with dimensions of 10.1 cm × 9.6 cm, as indicated by the arrow. This CT view is the coronal view. The pelvic collection displays different segments portraying different densities, as well as loculated portions as shown by the arrowhead.

wk after surgery. The ultrasonograms showed residual volumes of 53 mL at discharge; and 66 mL, 2 wk after surgery. However, the patient was clinically stable, and quite involved in her day-to-day activities. A follow up ultrasound done 2 mo after surgery showed complete resolution of the pelvic collection. The patient was then discharged from our surgical services.

DISCUSSION

Bacteria producing ESBLs were first described in Germany in 1983[28]. The ESBL enzymes hydrolyse the oxymino group on the beta-lactam cores of beta-lactam antibiotics[29]. The ESBL enzymes do not seem to have the ability to degrade carbapenems and cephamycins, which are structurally similar to cephalosporins, albeit

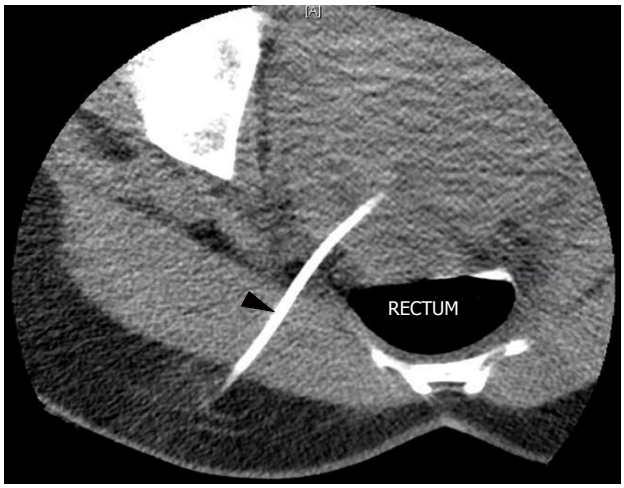

Figure 4 Percutaneous drainage of pelvic collection - axial view. The large pelvic collection (10.1 cm × 9.6 cm) was drained percutaneously under computerised tomography guidance, and an 8 French Pigtail drain was left in situ in the rectouterine pouch of Douglas, as evident by the radio-opaque linear object at the 7 o'clock position, as indicated by the arrowhead.

with increased anaerobic coverage[29]. The ESBLs are often encoded by large plasmids which also encode resistance to other antibiotics simultaneously, most commonly quinolones and aminoglycosides[2]. These transferrable bacterial plasmids confer multi-drug resistance to bacteria which host them, thereby limiting the repertoire of efficacious antibacterial options[30].

Nosocomial infections with ESBL *E. coli* are common worldwide[1]. The incidence of community-acquired infections with ESBL *E. coli* are also increasing worldwide[31]. The gastrointestinal tract is obviously the main reservoir for ESBL producing Enterobactericeae, including the notorious 2, *E. coli* and *Klebsiella*[5-7]. Colonisation is a strong risk factor for subsequent infection[5-7]. Travel to South Asia has emerged as a major risk factor for colonisation[5-7]. The unscrupulous misuse of antibiotics for traveller's diarrhoea in South Asia has only served to promote travel to South Asia as one of the most important risk factors for colonisation with ESBL Enterobacteriaceae[32,33]. Traditionally, colonisation has been iatrogenically associated with exposure to healthcare, as in the case of nosocomial infections during hospital stay[34]. More recently, community acquired ESBL bacterial infections have increased in incidence and prevalence, especially in the community setting of antimicrobial, immunosuppressive, and/or corticosteroid use[34].

The prevalence of ESBL-producing *E.coli* in acute appendicitis has been reported to be from 3.5% to 16.6%[35-37]. One study held ESBL E. coli accountable for 74.5% of isolated resistant bacteria isolated from acute appendicitis[38]. ESBL-producing E. coli can have a significant impact on the management of acute appendicitis. However there is scanty evidence describing the impact of ESBL-producing Enterobacteriaceae on appendiceal abscesses.

In this report, our patient developed a large postoperative pelvic abscess despite being on broad-spectrum antibiotics and a pelvic drain. The abscess was promptly identified, percutaneously drained and sent for culture and sensitivity. When the microbiology report identified ESBL-producing *E. coli* in the fluid drained, the patient was promptly treated with carbapenem under the guidance of the Infectious Diseases Specialists. The patient recovered and returned to her daily lifestyle quickly.

The choice of Polydioxanone Endoloop® or Endostapler did not seem to be influential in the pathogenesis of intraabdominal abscess. A retrospective study of 708 patients displayed a higher incidence (OR = 1.36) of developing intraabdominal abscess whilst using Endoloop®, when compared to Endostapler[39]. Conversely, a retrospective study involving 242 patients showed higher incidence of intraabdominal abscess when Endostapler was used in cases of perforated appendicitis, in contrast to when Endoloop® was used (OR = 7.09)[40]. However, a larger, better-designed, technically-superior, prospective study involving 1369 patients showed no difference in incidence of intra-abdominal abscess between Endoloop® use versus Endostapler use (OR = 0.96)[41]. Interestingly, using multivariable analysis, this prospective study also showed that complicated appendicitis was the only independent risk factor for an intraabdominal abscess (OR = 6.26)[41]. Another retrospective study showed no difference[42].

Although carbapenems like imipenem, meropenem, doripenem, and ertapenem are also antibiotics containing beta-lactam rings, they are the first-line option for treating ESBL bacteria. Ertapenem may be preferred for community-acquired infections due to its once-daily dosing regimen[43]. However, it is indeed noteworthy that perioperative appendicitis patients colonised with ESBL bacteria do not necessarily require cultures or specific antibiotics; unless there is a complication like abscess, perforation, or peritonitis[44].

Bacteria producing ESBLs are not widely considered in surgical prophylaxis or postoperative complications unless the patient is previously known to be colonised. This is the first case report on ESBL related surgical complications in a routine laparoscopic appendectomy published in a developed Western country[45]. There are currently 2 published case reports, one of which was 6-years-old and the other 9-years-old, describing patients with perforated appendicitis with an abscess due to ESBL-producing *E. coli*[26,27]. We had mentioned in the Methods section earlier that these 2 reports were from journals neither indexed in Pubmed nor from reputable publishing groups[26,27].

CONCLUSION

Our report is the first reliable report involving ESBL *E. coli* and appendiceal abscesses. This report is also the first one in a developed country involving ESBL *E. coli* related surgical complications in association with a routine laparoscopic appendectomy. In a major multicultural city like Sydney (our location), ESBL bacterial complications need to be carefully considered in perioperative infections, recalcitrant or otherwise. Moreover, surgical antimicrobial prophylaxis and guidelines may need to be reviewed, as ESBL bacterial infections become widespread.

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