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Septic shock after a saline infusion hysterosalpingosonogram in a woman with stage IV endometriosis and infertility: A case report

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ABSTRACT

Saline infusion sonohysterography/hysterosalpingo-contrast sonography is commonly used in the work-up of infertility. Overall, pelvic infection following these investigations is rare, but risk may be increased in patients with deep infiltrating endometriosis. Antibiotic prophylaxis is not professionally recommended in patients with advanced endometriosis, a point that requires reconsideration. A 29-year-old woman with stage IV endometriosis presented with pelvic inflammatory disease and sepsis following a saline hysterosalpingo-contrast sonogram for investigation of infertility. Her infection was resistant to antibiotic treatment and she required extensive surgical intervention for source control, which impacted her fertility. The immunodeficient pelvic microenvironment in patients with endometriosis and endometrioma can increase the risk and severity of pelvic infection. Antibiotic prophylaxis should always be utilized in those with stage IV endometriosis who are due to undergo saline infusion sonohysterography or hysterosalpingo-sonography.

1. Introduction

Saline infusion sonohysterography (SIS) and hysterosalpingo-contrast sonography (HyCoSy) are routinely used in the work-up of infertility. SIS and HyCoSy utilize a catheter to breech the cervix and introduce a small volume of sterile saline into the uterine cavity. This allows real-time ultrasound imaging to assess structural abnormalities of the endometrial cavity (SIS) and evaluate fallopian tube patency (HyCoSy).

Breeching the closed cervix has the potential to introduce vaginal microbes into the uterine cavity, posing an iatrogenic risk of pelvic inflammatory disease (PID) and tubo-ovarian abscess (TOA), though these are rare complications in the general population [1–3]. Nevertheless, the risk of infectious complications in women undergoing investigations for infertility is more than twice that of the general population [4]. The increased prevalence of underlying pelvic pathology in this population, such as endometriosis, may explain the elevated risk of infectious outcomes [5,6].

Prophylactic antibiotics in the form of doxycycline or azithromycin have come into favour among practitioners performing SIS/HyCoSy, in particular in patients with infertility, prior history of PID or hydrosalpinx [7]. Professional recommendations currently suggest antibiotic prophylaxis only for patients with dilated fallopian tubes [8]. Endometriosis, with or without the presence of an endometrioma, has not been identified in current guidelines as a risk factor indicating the need for antibiotic prophylaxis when SIS/HyCoSy is performed [6].

This report presents a case of septic shock following HyCoSy in a 29-year-old patient with primary infertility, known bilateral endometriomas and deep infiltrating endometriosis. The case discussion focuses on the aspects of management unique to PID in the context of deep endometriosis. Altered microbial environments and immune mechanisms, as well as unique surgical challenges, complicate the management of PID in this patient population. It also reviews appropriate antibiotic prophylaxis use when performing SIS/HyCoSy.

2. Case Presentation

The patient was a 29-year-old woman with primary infertility and deep infiltrating endometriosis with bilateral large endometriomas. A timeline of events is outlined in Table 1. Four years prior, fertility-preserving laparoscopic excision of endometriosis and left salpingectomy were performed. The medical history was otherwise significant for

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Table 1
Timeline of events. Day 0 represents admission to the emergency department.

−4 yrs	Initiated medical management for endometriosis with dienogest
−3 yrs	Laparoscopic excision of endometriosis, left salpingectomy, lysis of adhesions
−18 mo	Referred to reproductive endocrinology and infertility for primary infertility with background history of deep endometriosis
−6 days	HyCoSy and endometrial biopsy
Day 0	ED presentation with pelvic inflammatory disease and sepsis
+2 days	Laparoscopy converted to laparotomy with abdominal washout and debridement Tuberculosis and Group A strep ruled out
+3 days	Blood cultures on Day 0 speciated *Klebsiella*
+7 days	Repeat blood cultures on Day +3 negative Culture from OR on Day 2 resulted polymicrobial
+10 days	Repeat blood cultures on Day +6 negative New frank rectal bleeding
+11 days	Total abdominal hysterectomy, bilateral oophorectomy, right salpingectomy, bilateral ureterolysis, enterolysis, sigmoidoscopy, cystoscopy, repair of bladder cystotomy, right ureteric stent
+13 days	Cultures from OR Day +11 speciated *Candida* Repeat blood cultures Day +9 negative Respiratory cultures positive for yeast
+17 days	Post-op ileus 18 cm intra-abdominal abscess, percutaneous drain placed by interventional radiology
+21 days	Ileus resolved
+24 days	Successful trial of void, CT urogram normal
+27 days	Percutaneous drain removed
+31 days	Discharged from hospital, to continue IV antibiotics with close follow-up

type 2 diabetes mellitus treated with insulin, elevated body mass index, fatty liver disease and recent hospitalization for proctitis, suspected to be secondary to inflammation caused by deep infiltrating endometriosis.

The patient presented to hospital with significant abdominal pain and fever six days after an endometrial biopsy and HyCoSy were performed for fertility work-up. She had taken five days of azithromycin prophylaxis for the procedure, as prescribed.

Palpation of the uterine fundus, cervix and bilateral adnexa elicited tenderness. The patient became febrile and vitally unstable with significant tachycardia above 130 bpm. Investigations demonstrated leukocytosis (17.4×10^9/L) and elevated CRP (343.2 mg/L). Transvaginal ultrasound showed bilateral endometriomas, enlarged from prior imaging, an endometriosis nodule at the retrocervix, and new right hydroureteronephrosis. A preliminary diagnosis was made of septic shock secondary to PID following recent HyCoSy. While there was no sonographic evidence of TOA, at least one endometrioma was presumed to be the source of infection.

Despite broad-spectrum coverage with pipercillin-tazobactam and vancomycin, the patient was persistently febrile, tachycardic, tachypneic and hypoxic. Leukocytosis was also persistent and labs revealed acidosis.

Forty-eight hours after initial presentation, cultures remained pending. Given failure of broad-coverage antibiotics and ongoing septic shock, surgical intervention was recommended. Operative goals included obtaining source control while preserving fertility. The surgical plan was for a midline laparotomy and unilateral salpingo-oophorectomy. On entry into the abdomen, a cemented pelvis was encountered with massive inflammatory fibrin deposits and dense inflammatory bowel adhesions. The patient was hemodynamically compromised throughout the procedure. To shorten the surgical time and preserve fertility, the intervention performed was a midline laparotomy, lysis of adhesions and abdominal washout. The patient was transferred to the intensive care unit (ICU) postoperatively. Cultures obtained from this procedure resulted polymicrobial.

Given the hostile abdomen encountered at surgery, the management plan shifted to prolonged intravenous antibiotic therapy. The goal was to reduce acute inflammation, reverse signs of shock and perform interval unilateral salpingo-oophorectomy for definitive source control, while preserving one ovary.

Despite showing initial improvement, the patient's pain worsened and she was persistently tachypneic, tachycardic and febrile with worsening leukocytosis. On day 11 of admission, after extensive discussion around fertility and clear antibiotic resistance, the patient underwent total abdominal hysterectomy, bilateral oophorectomy, right salpingectomy, bilateral ureterolysis, enterolysis, sigmoidoscopy, cystoscopy, and repair of bladder cystotomy. Following this procedure, she began to show clinical improvement with normalizing vital signs, and was transferred out of the ICU on post-operative day 3. Cultures from this second procedure speciated *Candida* and fluconazole was added.

The post-operative course was prolonged, complicated by ileus and a new intra-abdominal abscess, which was drained percutaneously and resolved prior to discharge. The patient was discharged on post-operative day 23, admission day 31. Intravenous antibiotics were continued for a short period after discharge, following recommendations by the infectious disease team. The patient was seen in clinic six weeks after discharge and was doing well. Given premature iatrogenic menopause, topical and vaginal estradiol were initiated for hormone replacement, which was well tolerated. The patient declined to share a patient perspective for the purpose of this report.

3. Discussion

Only a few cases in the literature report severe PID following SIS/HyCoSy [1–3]. This particular case presented a number of management challenges that might apply for other patients with advanced endometriosis with severe, life-threatening sepsis and PID. It also highlights consideration of appropriate antibiotic prophylaxis for fertility investigations in this patient population, as well as consideration of the necessity of invasive testing that may instigate serious infection.

Patients with endometriosis undergoing fertility procedures have an elevated risk of developing PID from egg retrievals and intrauterine manipulation, which may be secondary to the unique pelvic microenvironment [9–11]. Campos et al. (2018) identified that *M. genitalum* is present in the pelvic environment of endometriosis patients and is shown to down-regulate immune function and potentiate inflammation in endometriosis [12]. Similarly, *E. coli* is found in menstrual blood and endometriosis deposits in those with endometriosis, suggesting an altered microbial environment [11,13]. When cultured, *E. coli* grew in 43 % of TOAs in patients with endometriosis compared with 17 % in non-endometriosis TOAs [6]. This data suggests that altered microbial flora unique to endometriosis puts these patients at risk for increased incidence of infection, prolonged infectious courses and increased risk of fastidious bacteria. First-line antibiotics for the treatment of PID and antibiotic prophylaxis prior to invasive investigations in this patient population should include broad gram-negative and anaerobic coverage, such as third-generation cephalosporins and metronidazole.

Endometriosis is a pro-inflammatory disease with immunodeficient characteristics that can increase the likelihood and severity of PID [14]. The immunological hypothesis that forms the basis of endometriosis pathophysiology suggests that those with the disease have impaired innate immune function. Increased macrophage production of proinflammatory cytokines such as TNFa, IL-6 and IL-1B, as well as reduced natural killer cell function, are well documented in endometriosis [15]. In this way, endometriotic deposits evade immune surveillance, a mechanism that can be projected to a developing pelvic infection. The presence of an endometrioma is an independent risk factor for the development of TOA [5,6]. Endometrioma increases the risk of TOA, in addition to antibiotic treatment resistance and increased need for surgical intervention [16]. The thin endometrial cyst barrier is prone to bacterial penetration, chocolate cyst fluid provides a rich culture

medium, and the physiologic immunocompromised environment decreases host defences [6]. These mechanisms work in conjunction to elevate the risk of PID and severity of PID in patients with endometriosis.

Severe PID and TOA in patients with endometriosis are less likely to improve on broad-spectrum antibiotics alone and are more likely to require surgical intervention than those without endometriosis [9,16–18]. The combination of PID and severe endometriosis greatly elevates surgical difficulty, risk of postoperative complication and risk of surgical sterility. These patients also have longer operative times and hospital stays [17]. Even without active infection, surgery for advanced endometriosis poses an increased risk of complications pertaining to the surgical difficulty, with one series reporting up to 11.76 % [19]. Rates of postoperative complications following surgery for PID in patients with and without endometriosis were similar. However, when broken down, bowel and urologic complications were more common in those with endometriosis [17]. Clarizia, et al. (2021) report a complication rate of 7.6 % following surgical intervention for emergency management of PID in patients with endometriosis. They also report an increased likelihood of salpingectomy associated with the presence of endometriosis at the time of surgery for PID [17]. Presence of endometriosis, in particular endometrioma, increases the risk of surgical intervention for management of severe PID and TOA, and surgical challenges must be considered in surgical planning and patient consent. Furthermore, the possible result of early menopause and menopausal management must also be considered. A holistic approach with estrogen and progesterone replacement as well as consideration of bone and cardiovascular health should be included in management [20].

4. Conclusion

Although rare, infection following SIS/HyCoSy has been documented [1–4]. Currently, guidelines do not support universal prophylaxis prior to these procedures, unless certain risk factors exist. Those risk factors do not include stage IV endometriosis, despite the risk of developing PID and TOA with pre-existing endometriosis. Furthermore, the altered pelvic microenvironment in endometriosis warrants reconsideration of the choice of antibiotic prophylaxis for patients presenting for SIS/HyCoSy with a known history of deep endometriosis and endometriomas. Prior to SIS/HyCoSy, the practitioner and patient should evaluate the necessity of the test and have a comprehensive discussion of the risks.

Contributors

Mariah Colussi contributed to patient care, conception of the case report, acquiring and interpreting the data, drafting the manuscript, undertaking the literature review and revising the article critically for important intellectual content.

Geneviève Horwood contributed to patient care, conception of the case report, acquiring and interpreting the data, drafting the manuscript, and revising the article critically for important intellectual content.

Jenn McCall contributed to drafting the manuscript and revising the article critically for important intellectual content.

Jenna Gale contributed to patient care, conception of the case report and revising the article critically for important intellectual content.

Sukhbir Singh contributed to patient care, conception of the case report and revising the article critically for important intellectual content.

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During the preparation of this work the authors used ChatGPT in order to rephrase highlights to satisfy the character count. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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The authors declare that they have no conflict of interest regarding the publication of this case report.

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