

Pyomyoma: Case Report and
Comprehensive Literature Review of 75
Cases Since 1945Obteene Azimi-Ghomi^{1*} and Jeremy Gradon²¹University of Medicine and Health Sciences, Sinai Baltimore Hospital, USA²Sinai Baltimore Hospital, USA

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Abstract

Pyomyoma is a rare and potentially fatal suppurative complication of leiomyoma, with less than 100 known cases reported since it was first described in literature in 1871. A case is described of the presentation, management, and outcome of a patient who developed a pyomyoma following a septic abortion and uterine instrumentation. We then perform an extensive literature review encompassing 75 known reported cases of pyomyoma since 1945, analyzing 10 different factors, including patient age, pregnancy and menopausal status, clinical presentation, known etiological causes, isolated causative organisms, blood culture results, presence of leukocytosis, treatment implemented, and patient survival. This review will help to further expound on and characterize pyomyomas, allowing for better understanding of the condition and improved clinical assessment and patient management in the future.

Introduction

Leiomyomas are the most common neoplasm found in women [1]. Studies have shown that by age 50, approximately 70% of Caucasian females, and 80% of females of African origin suffer from leiomyomas [1,2]. An increased incidence of leiomyomas has been noted to occur in women with obesity, nulliparity, early menarche, a family history of leiomyoma, and those of Afro-Caribbean ethnicity [2-4].

Pyomyoma, also known as Suppurative Leiomyoma, is a very rare yet potentially lethal complication of uterine leiomyoma. Pyomyomas are thought to arise secondary to infarction and degeneration of a pre-existing leiomyoma, which is then seeded with bacteria and subsequently becomes infected [5]. Pyomyomas are most commonly seen during or soon after pregnancy, due to hemorrhage and necrosis of the fibroid, as well as during the post-menopausal period, secondary to vascular insufficiency [2,5]. Pyomyomas have also been known to occur following uterine instrumentation, such as during dilatation and curettage, as well as cesarean section delivery, both of which can introduce microorganism into the uterine cavity [5,6]. Sub mucosal leiomyomas are most commonly infected due to their close proximity with the uterine cavity and their tenuous blood supply compared to other types of leiomyomas, both characteristics that increase the risk for necrosis and subsequent infection to develop [5].

Case Report

A 32 year old G2P0010 African American female presented to the ED with complaints of pelvic pain and vaginal bleeding of sudden onset. The patient was at the time 12 weeks pregnant. Pelvic ultrasound and speculum examination determined that the patient was had an incomplete abortion with passage of fetal tissue during that visit. She was discharged with instructions to follow up with her Ob-Gyn. 2 days later, the patient returned with complaints of fevers, chills, worsening pelvic pain, and heavy vaginal bleeding. T_{max} of 40.7 C and Leukocytosis were seen. Ultrasound (U/S) determined presence of retained products of conception along with multiple leiomyomas, and a diagnosis of septic abortion was made. The patient underwent an emergent Dilatation and Curettage (D & C) with uterine evacuation of products of conception. Blood cultures drawn revealed the presence of *Bacteroides fragilis* bacteremia, and the patient was placed on a post-operative course of IV Ampicillin-Sulbactam until resolution of fever and sterile blood culture results were obtained, followed by discharge on 2 week course of PO Amoxicillin-Clavulanate. The patient continued to experience pelvic discomfort, and upon completion of the antibiotics, began experiencing spiking fevers, as well as progressively increasing abdominal pain. The patient also complained of dysuria and pain with urination. 'Cottage cheese' discharge was present. Leukocytosis was seen on CBC. A pelvic sonogram was performed that demonstrated a 6 x 6 x 6 cm heterogeneous mass. A repeat dilation and curettage with U/S guidance was performed which demonstrated the mass to be a degenerating leiomyoma that was previously noted on Pelvic U/S. Tissue cultures of the leiomyoma and blood cultures returned positive for *B. fragilis*, and IV Zosyn was initiated. MRI of the Pelvis

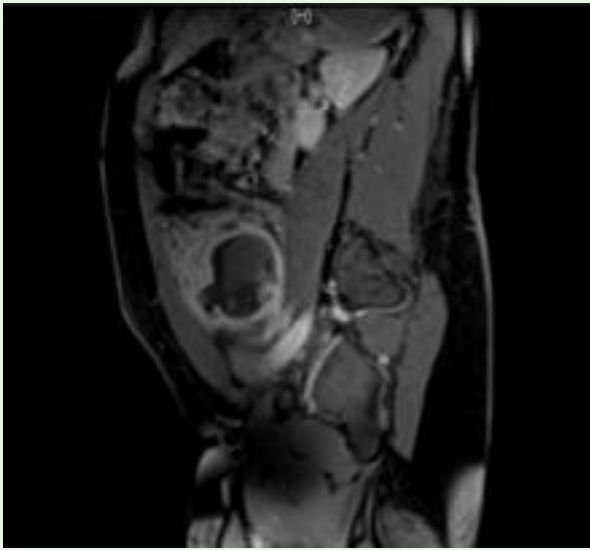


Figure 1: Abdominal and Pelvic MRI of the Pyomyoma, demonstrating heterogeneity within the mass, presence of an enhancing peripheral rim, and a partial capsular rupture at the anterior aspect.

was performed demonstrating a large 7 cm hemorrhagic and necrotic leiomyoma with partial rupture and associated inflammatory changes (Figure 1). No abscess or fluid collection was seen. A second, smaller infarcted leiomyoma was also observed (Figure 1). The patient was subsequently diagnosed with a pyomyoma. The patient refused surgical removal of the leiomyoma due to the possible risk of conversion to hysterectomy, as the patient planned on conceiving in the future. She was maintained on IV Zosyn until conversion of blood cultures to sterility, and discharged again on a course of PO Augmentin. At follow-up one month after discharge, the patient was doing well clinically and without symptoms.

Literature Review

Methods

Since 1945, there have been 75 reported cases of pyomyoma, including our current case. In our extensive literature review of these cases, we aim to elucidate the epidemiological characteristics of these 75 patients diagnosed with pyomyoma (Table 1). Ten characteristics of each case are analyzed and determined: patient age, association of pyomyoma with pregnancy, presence of menopause, known cause of pyomyoma, presenting symptoms, isolated organism, status of blood cultures, presence of leukocytosis, treatment received by patient, and patient survival/mortality (Table 1). MEDLINE, Pub med, OMICS, and Google Scholar were utilized in the search for cases of pyomyoma. All case reports detailed between 1945 and 2017 were included in the review, with the 10 characteristics compiled into a table (Table 1). The absences of any of the specific characteristics to be studied were noted by the presence of 'Unknown/Not Stated' within the table (Table 1).

Results

75 cases of pyomyoma gathered from an extensive review of the existing literature since 1945 were analyzed (Table 1). Patient ages ranged from 22 to 75 years of age. Of the 75 patients diagnosed with pyomyoma, 36 cases were associated with pregnancy. The ages of

these patients ranged from 22 to 44 years, with an average age of 33.1 years. Of the 39 cases not associated with pregnancy, an age range of 24 to 75 years with an average age of 48.6 years was seen. Of the 75 cases reviewed, 19% (14/75) were associated with known post-menopausal patients.

The cause of pyomyoma was known in only 76% of cases (57/75). In the 18 cases of pyomyoma with an unknown etiological cause, all were seen in non-pregnancy associated patients (Table 1). In the 57 cases of pyomyoma with a known cause, 26% (15/57) were attributed to abortions/miscarriages, with 2/3rd of these cases (10) associated with uterine instrumentation, most commonly using dilation and curettage (D & C). Spontaneous abortions were the most commonly encountered type, at 6 total cases, followed by Induce abortions (4), Septic abortions (2), Missed abortions (2), and a single case of incomplete abortion with D & C (Table 1). Uterine Artery Embolization (UAE) was the causative mechanism in 23% of cases (13/57). Delivery of a pregnancy was associated with the cause of pyomyoma in 28% of cases (16/75); 7 of these cases involved a cesarean section (12% overall), with the remaining being vaginal deliveries (16% overall). Lesser common causes of Pyomyoma included Chorioamnionitis and Intrauterine Devices (IUD), each associated with 5% (3/57) of pyomyoma with a known cause. Of note, one case of an IUD-caused pyomyoma was also associated with a pregnant patient, who also resulted in miscarriage of the fetus, and one case of chorioamnionitis-induced pyomyoma was associated with intra-uterine balloon usage, a type of uterine instrumentation, to control post-partum hemorrhage [16,65]. The remaining causes of pyomyoma, attributing for a single each, included Intravenous Drug Abuse (IVDA), unsterile herbal remedy Intravenous injection, endocarditis, infectious pancreatitis, and an ascending genital tract infection [5,18,20,22,63].

Pyomyomas reviewed in the 75 cases presented in a broad variety of manners (Table 1). The 3 most common presentations were fever in 87% (65/75); pelvic and/or abdominal pain in 75% (56/75); and presence of an abdominal and/or pelvic mass, in 27% (20/75) of cases (Figure 2). Vaginal discharge or bleeding was seen in 21 % (16/75), Nausea/Vomiting was present in 15% (11/75), and fatigue/weakness/lethargy in 8% (6/75) of cases (Figure 2). Other less common symptoms included change in bowel habits 7% (5/75), Weight loss 5% (4/75), and fistulous drainage from the abdomen 4% (3/75). Changes in menstrual habits, including dysmenorrhea and menorrhagia, were present in 3 of the 36 non-menopausal cases, and 4% of overall cases.

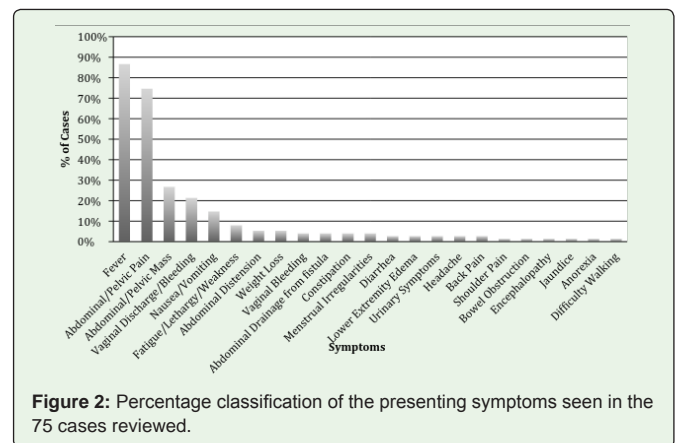


Figure 2: Percentage classification of the presenting symptoms seen in the 75 cases reviewed.

Table 1: Compilation of details and analysis of 75 reviewed cases in literature since 1945.

Abx: Antibiotics; Abd: Abdominal; IVDA: Intra-Venous Drug Abuse; TAH: Total Abdominal Hysterectomy; BSO: Bilateral Salpingo-Oophorectomy; RSO: Right Salpingo-Oophorectomy; LSO: Left Salpingo-Oophorectomy; *E. coli*: *Escherichia coli*; *S. aureus*: *Staphylococcus aureus*; Spp.: Species; IUD: Intra-Uterine Device; D&C: Dilatation and Curettage; GNR: Gram Negative Rods; U/S: Ultrasonography

Case	Age	Assoc. with pregnancy	Menopause	Cause	Symptoms	Organism	Blood Cultures	Leukocytosis	Treatment	Outcome
Miller 1945 [7]	51	No	Yes	Unknown	Fever, Abd Pain, Abd Mass	<i>Streptococcus hemolyticus</i>	Negative	Yes	Abx + Subtotal TAH/BSO	Died
Bedrosian et al. 1956 [8]	50	No	Yes	Unknown	Abd Pain (presenting as Acute Abdomen)	Coliform group	Unknown	Yes	Abx + TAH/BSO	Survived
Dubois/Neumann 1957 [9]	29	Yes	No	Pregnancy/Delivery	Fever, Abd Pain	Unknown/Not Stated	Unknown	Yes	Abx + Vaginal Expulsion/Myomectomy	Survived
Ruch 1963 [10]	34	Yes	No	Pregnancy/Delivery	Fever, Abd Pain, Headache	Coag-Neg. <i>Staphylococcus</i>	Unknown	Yes	Abx + TAH/BSO	Survived
Kaufman et al. 1974 [11]	58	No	Yes	Unknown	Fever, Jaundice	<i>Clostridium perfringens</i>	Positive	Yes	Abx only	Died
Weiss et al. 1976 [12]	59	No	Yes	Unknown	Fever, Weight Loss, Abd Drainage from fistula	Polymicrobial (<i>Proteus</i> spp, <i>Clostridium</i> spp, <i>Enterobacteriaceae</i> , <i>Streptococcus</i> spp)	Unknown	Unknown	Abx + TAH/BSO + Fistula closure	Survived
Feeney et al. 1979 Case #1 [13]	37	Yes	No	Spontaneous Abortion	Fever, Nausea, Vomiting, Diarrhea, Bowel Obstruction	<i>Bacteroides fragilis</i>	Unknown	Unknown	Abx + TAH	Survived
Feeney et al. 1979 Case #2 [13]	35	Yes	No	C-section/Pregnancy	Fever	<i>Bacteroides fragilis</i>	Unknown	Unknown	Abx only	Survived
Fuller et al. 1985 [14]	68	No	Yes	Unknown	Abd Mass, Pedal Edema	<i>Streptococcus</i> spp	Negative	Yes	Abx + TAH/BSO	Survived
Prichard et al. 1986 [15]	37	Yes	No	Spontaneous Abortion	Fever, Pelvic/Abd Pain	<i>Streptococcus milleri</i>	Positive	Yes	Abx + TAH/BSO	Survived
Wong et al. 1986 [16]	29	Yes	No	IUD (IUD-induced abortion)	Fever, Abd Pain, Vaginal Bleeding, Uterine Tenderness	Polymicrobial (<i>S. aureus</i> , <i>Serratia marcescens</i>)	Negative	Yes	Abx + TAH/BSO	Survived
Greenspoon et al. 1990 [5]	49	No	No	Unsterile IV Injection of Herbal Remedies (Apricot pit juice)	Fever, Abd Pain, Weight Loss, Encephalopathy	Polymicrobial (<i>Enterococcus</i> spp., <i>Staphylococcus aureus</i> , <i>Actinomyces meyeri</i>)	Positive	Yes	Abx only	Died
Das et al. 1994 [6]	44	Yes	No	Induced Abortion/Uterine Instrumentation	Fever, Abd Pain	<i>E. coli</i>	Negative	Yes	Abx + TAH/BSO	Survived
Tobias et al. 1996 [17]	32	Yes	No	Induced Abortion/Uterine Instrumentation	Fever, Abd Pain, Nausea/Vomiting	<i>Enterococcus faecalis</i>	Negative	Yes	Abx + TAH/BSO	Survived
Prahlow et al. 1996 [18]	31	Yes	No	secondary Septic Abortion	Abd Pain, Constipation	<i>S. aureus</i>	Positive	Yes	Abx + TAH/BSO	Survived
Gupta et al. 1999 [19]	75	No	Yes	Unknown	Fever, Abd Mass	<i>Streptococcus</i> spp.	Negative	Yes	Abx + U/S guided Aspiration	Survived
Yang/Wang 1999 [20]	46	No	No	Acute Infectious Pancreatitis	Fever, Abd Pain	<i>Edwardsiella elliottii</i>	Positive	Yes	Abx + TAH/BSO	Survived
Grune et al. 2001 [21]	44	Yes	No	Pregnancy	Fever	<i>Klebsiella pneumoniae</i>	Positive	Yes	Abx + Myomectomy	Survived
Genta et al. 2001 [22]	60	No	Yes	Endocarditis	Fever, Abd Mass, Weakness, Anorexia, Weight Loss	<i>Strep agalactiae</i>	Positive	Yes	Abx + TAH/BSO	Survived
Lohle et al. 2001 [23]	N/A	No	No	Uterine A. Embolization	Fever	Unknown	Negative	Yes	Abx + TAH	Survived
Lin et al. 2002 [24]	33	Yes	No	C-section/Pregnancy	Fever, Abd Pain	<i>Candida parapsilosis</i> (Blood Culture: <i>E. coli</i>)	Positive (<i>E. coli</i>)	Yes	Abx + TAH/BSO	Survived
Huang et al. 2003 [25]	41	No	No	Uterine Artery Embolization	Fever, Abd Pain, Vaginal Discharge	<i>E. coli</i>	Positive	Yes	Abx + Manual Removal of fibroid	Survived
Karcaaltincaba et al. 2003 [26]	36	Yes	No	Septic Abortion (without D & C)	Fever, Abd Pain	<i>Peptostreptococcus tetradus</i>	Positive	Yes	Abx + Myomectomy	Survived
Aungst et al. 2004 [27]	39	No	No	Uterine Artery Embolization	Fever, Abd Pain, Vaginal Bleeding	Polymicrobial (<i>Fusobacterium necrophorum</i> , <i>Corynebacterium</i> spp, <i>Bacteroides</i> spp.)	Positive	Yes	Abx + TAH/BSO	Survived
Sahet et al. 2005 [28]	64	No	Yes	Unknown	Fever, Abd Pain	<i>S. aureus</i>	Negative	Yes	Abx + TAH/BSO	Survived
Ojabo et al. 2005 [29]	33	No	No	Unknown	Fever, Abd Pain, Abd Mass, Nausea, Vomiting	<i>S. aureus</i>	Negative	Yes	Abx + Myomectomy	Survived
Mason et al. 2005 [30]	29	Yes	No	Pregnancy/Delivery/Post-partum period	Fever, Abd Pain, Abd Mass, Nausea/Vomiting, Dysuria	No Organism isolated	Negative	Yes	Abx + Myomectomy	Survived
Yeate et al. 2005 [31]	53	No	Yes	Unknown	Fever, Abd Pain, Abd Distension, Abd Mass, Nausea, Vomiting, Constipation, Weight Loss	<i>Proteus mirabilis</i>	Negative	Yes	Abx + TAH/BSO	Survived

Kitamura <i>et al.</i> 2005 [32]	N/A	No	Unknown	Uterine Artery Embolization	Not Stated	Unknown/Not Stated	Unknown	Unknown	Abx + TAH/BSO	Survived
Jaishuenet. <i>al.</i> 2006 [33]	57	No	Yes	Unknown	Fever, Abd Pain, Abd Mass, Abd Distension	No Organism isolated	Negative	No	Abx + TAH/BSO	Survived
Calleja-Agiuset. <i>al.</i> 2006 [34]	30	Yes	No	Pregnancy/C-section	Fever, Abd Pain, Abd Mass	<i>E. coli</i>	Negative	Yes	Abx + Myomectomy + Appendectomy	Survived
Fioriet. <i>al.</i> 2006 [35]	N/A	No	Unknown	Uterine Artery Embolization	Fever, Abd/Pelvic Pain, Vaginal Discharge	<i>E. coli</i>	Negative	Yes	Abx + Manual Removal on Vaginal exam	Survived
Manchanaet. <i>al.</i> 2007 [36]	42	No	No	IUD	Fever, Abd Pain, Abd Mass	Anaerobic GNR	Negative	Yes	Abx + TAH/BSO	Survived
Patwardhanet. <i>al.</i> 2007 [37]	38	No	No	Torsion of Pedunculated Myoma	Fever, Abd Pain	<i>S. aureus</i>	Negative	Yes	Abx + Myomectomy	Survived
Vuralet. <i>al.</i> 2007 [38]	24	No	No	Uterine Artery Embolization	Abd Pain, Vaginal Discharge	Unknown/Not Stated	Unknown	No	Abx + Fistula repair	Survived
Nguyen <i>et al.</i> 2008 [39]	40	Yes	No	Chorioamnionitis	Fever, Abd Pain	<i>E. coli</i>	Positive	Yes	Abx + TAH	Survived
Mubarak <i>et al.</i> 2008 [40]	52	No	Yes	Unknown	Fever, Abd Pain, Abd Mass, Bilat Lower Ext Edema	Unknown/Not Stated	Negative	Yes	Abx + Percutaneous Aspiration and U/S guided Drainage	Died
Fletcher <i>et al.</i> 2009 [41]	44	No	No	Unknown	Fever, Abd Pain, Abd Mass, Vaginal Discharge, Vomiting, Diarrhea	Methicillin-resistant Staph epidermidis (MRSE)	Positive	Yes	Abx + Subtotal Hysterectomy/BSO	Survived
Nunez <i>et al.</i> 2010 [42]	29	Yes	No	Septic Abortion/ D & C	Fever, Abd Pain, Cervical Motion Tenderness, Vaginal Discharge/ Bleeding, Nausea,	Gram Pos. Cocci (unspecified)	Positive	No (Leukopenia)	Abx + TAH/BSO	Survived
Abulafiaet. <i>al.</i> 2010 [43]	48	No	No	Uterine Artery Embolization	Fever, Pelvic/Abd Pain	<i>E. coli</i>	Negative	Yes	Abx + TAH	Survived
Lee <i>et al.</i> 2010 [44]	46	No	No	Unknown	Fever, Abd Mass	Unknown/Not Stated	Unknown	No	Abx + TAH/LSO	Survived
Kuriyamaet. <i>al.</i> 2010 [45]	51	No	No	Unknown	Fever, Lower Back Pain	Anaerobic GNR	Unknown	Yes	Abx + TAH	Survived
Chen <i>et al.</i> 2010 [46]	46	No	No	Unknown	Fever, Menorrhagia, Dysmenorrhea, Abd Mass	<i>E. coli</i>	Negative	Yes	Abx + TAH	Survived
Zanganehet. <i>al.</i> 2010 [47]	47	No	No	Unknown	Fever, Shoulder Pain	Citrobacter spp.	Negative	No	Abx + TAH/ BSO	Survived
Shaabanet. <i>al.</i> 2011 [48]	30	Yes	No	Pregnancy/C-section	Fever, Abd Pain, Abd Mass, Fistula with Abdominal purulent drainage	<i>Staphylococcus lugdunensis</i>	Unknown	Unknown	Abx + Myomectomy and Fistula Repair	Survived
Liu <i>et al.</i> 2011[49]	42	No	No	Unknown	Fever, Abd Pain	Unknown/Not Stated	Unknown	Yes	Abx + Surgical Drainage and Marsupialization	Survived
Stroumsaet. <i>al.</i> 2011 [50]	41	Yes	No	Induced Abortion/Uterine Instrumentation	Fever, Abd Pain, Abd Mass	<i>Clostridium perfringens</i>	Positive	Yes	Abx only	Survived
Laubachet. <i>al.</i> 2011 Case #1 [51]	31	Yes	No	Missed Abortion/ D & C	Fever, Abd Pain	<i>E. coli</i>	Positive	No	Abx + CT-guided drainage	Survived
Laubachet. <i>al.</i> 2011 Case #2 [51]	35	Yes	No	Chorioamnionitis& C-section	Fever, Abd Pain	Polymicrobial (<i>E. coli</i> , <i>Candida albicans</i> , <i>Candida dubliniensis</i>)	Negative	Yes	Abx + CT-guided drainage	Survived
Laubachet. <i>al.</i> 2011 Case #3 [51]	31	Yes	No	Spontaneous Abortion/ D & C	Fever, Abd Pain	Polymicrobial (<i>Enterococcus faecalis</i> , <i>Streptococcus</i> spp.)	Negative	Yes	Abx + CT-guided drainage-Subtotal Abdominal Hysterectomy	Survived
Pinto <i>et al.</i> 2012 [52]	37	No	No	Uterine Artery Embolization	Fever, Abd Pain	<i>Propionibacterium acnes</i>	Negative	No	Abx + Laparoscopic Drainage	Survived
Shuklaet. <i>al.</i> 2012 [53]	65	No	Yes	Uterine Artery Embolization	Fever, Abd Pain, Abd Mass	<i>Enterococcus faecalis</i>	Negative	No	Abx + TAH/BSO	Survived
Golet. <i>al.</i> 2012 [54]	22	Yes	No	C-section/ Pregnancy	Abd Pain Nausea, Vomiting	No Organism isolated	Negative	Yes	Abx + Myomectomy	Survived
Sirhaet. <i>al.</i> 2013 [55]	37	Yes	No	Pregnancy/C-section; PPROM	Fever, Abd Pain, Vomiting	No Organism isolated	Negative	Yes	Abx + TAH	Survived
Rosen <i>et al.</i> 2013 [56]	47	No	No	Uterine Artery Embolization	Fever, Abd Pain	Polymicrobial (<i>S. aureus</i> , Coag-Neg. Staph, <i>Prevotellamelaninogenica</i>)	Positive	Yes	Abx + Subtotal Hysterectomy/RSO	Survived
Kobayashi <i>et al.</i> 2013 [57]	28	Yes	No	Pregnancy	Fever, Abd Pain, Vaginal Discharge	Anaerobic GNR	Negative	Yes	Abx + Myomectomy	Survived
Ugurlicanet. <i>al.</i> 2013 [58]	31	Yes	No	Missed Abortion/ D & C	Fever, Abd Pain, Vaginal Discharge	<i>Enterococcus faecalis</i>	Negative	Yes	Abx + Myomectomy	Survived
Shiotaet. <i>al.</i> 2013 [59]	36	Yes	No	C-section/ Pregnancy	Fever, Abd Pain, Vaginal Fluid/Discharge	<i>Enterococcus faecalis</i>	Negative	Yes	Abx + Myomectomy	Survived
Del Borgoet. <i>al.</i> 2013 [60]	37	Yes	No	Pregnancy	Fever, Abd Pain	<i>Sphingomonas paucimobilis</i>	Positive	Yes	Abx + Myomectomy	Survived
Ono <i>et al.</i> 2014 [61]	69	No	Yes	Unknown	Pelvic Discomfort, Fatigue	<i>Pasteurella multocida</i>	Negative	No	Abx + TAH	Survived
Magroet. <i>al.</i> 2014 [62]	33	Yes	No	Pregnancy/ Delivery	Fever, Abd Pain, Abd Mass, Lethargy	<i>Atopobium vaginae</i>	Negative	Yes	Abx + Surgical Drainage	Survived

Gupta et. al. 2014 [63]	35	No	No	Ascending genital tract infection	Fever, Abd Mass	<i>E. coli</i>	Negative	Yes	Abx + Myomectomy	Survived
Goyal et. al. 2014 [64]	42	No	No	Tubo-ovarian Abscess	Menorrhagia	Unknown/Not Stated	Negative	No	Abx + Subtotal Hysterectomy/LSO	Survived
Kaler et. al. 2015 [65]	28	Yes	No	Chorioamnionitis	Fever, Abd Pain, Lethargy, Vaginal Discharge	<i>E. coli</i>	Negative	Yes	Abx + Myomectomy	Survived
DeMaio et. al. 2015 [66]	N/A	Yes	No	Pregnancy/Delivery/Post-partum period	Fever, Abd Pain, Vaginal Discharge	Anaerobic GNR	Positive	Yes	Abx + Manual removal	Survived
Adeoye et. al. 2015 [67]	26	Yes	No	Spontaneous Abortion	Fever, Abd Pain, Abd Distension, Vomiting, Constipation, Vaginal Discharge	Anaerobic Gram Pos Cocci	Negative	No	Abx + Myomectomy	Survived
Rezaei et. al. 2016 Case #1 [68]	46	No	No	Uterine Artery Embolization	Fever, Abd Pain, Back Pain, Vaginal Discharge	<i>E. coli</i>	Negative	No	Abx + TAH/BSO	Survived
Rezaei et. al. 2016 Case #2 [68]	35	No	No	Uterine Artery Embolization	Fever, Abd Pain, Nausea, Vomiting, Diarrhea, Headache, Weakness	<i>E. coli</i>	Negative	Yes	Abx + TAH	Survived
Bhave et. al. 2016 [69]	35	Yes	No	Pregnancy/Delivery	Fever, Abd Mass	Unknown/Not Stated	Negative	Yes	Abx + Myomectomy	Survived
Naiyukiet. al. 2016 [70]	53	No	Yes	IUD	Abd Distention, Weakness, Difficulty walking	<i>Streptococcus agalactiae</i>	Negative	Yes	Abx + TAH/BSO	Survived
Rajalakshmi et. al. 2016 [71]	42	Yes	No	Incomplete Abortion/ D & C	Fever, Abd Pain, Umbilical fistula with drainage	<i>E. coli</i>	Negative	Yes	Abx + TAH/BSO + Fistulectomy	Survived
Obele et. al. 2016 [72]	37	No	No	Uterine Artery Embolization	Meno-metrorrhagia, Urinary Frequency,	Anaerobic Gram Pos. Cocci	Positive	Yes	Abx + Subtotal Hysterectomy/BSO	Survived
Pintonet. al. 2016 [73]	28	Yes	No	Spontaneous Abortion	Fever, Abd/Pelvic Pain, Vaginal Discharge, Abd Mass	No Organism isolated	Negative	Yes	Abx + Myomectomy	Survived
Bagga et. al. 2017 [74]	26	Yes	No	Spontaneous Abortion/ D & C	Fever	<i>E. coli</i>	Negative	Yes	Abx + Myomectomy	Survived
Current Case	32	Yes	No	Septic Abortion/ D & C	Fever, Abd Pain	<i>Bacteroides fragilis</i>	Positive	Yes	Abx only	Survived

The causative organisms in the majority of cases reviewed were ascertained by either microbiological assessment of the pus obtained from the pyomyomas, or pathological examination of the leiomyoma and/or uterine specimens removed following surgical treatment. Nine of 75 cases reviewed had no mention of a known causative organism (Table 1). In the remaining 66 cases, 8% (5/66) had no isolated causative organism following microbiological testing with gram stain and culture of pyomyoma tissue and pus, and 92% (61/66) had an isolated organism(s) (Table 1).

Of these 61 cases with a known microbiological cause, 54 of these cases (88.5%) were due to a single microorganism, and the remaining 7 cases (11.5%) were polymicrobial (Table 1). The most common causative organism isolated was *Escherichia coli*, seen in 15 total cases (25%), followed by Staphylococcal species (11 cases; 18%), Streptococcal species (8 cases; 13%), and Enterococcal species (7 cases; 11%). *Staphylococcus aureus* comprised 7 of the 11 total staphylococcal organisms present. Specific streptococcal species present included *S. milleri*, *S. hemolyticus*, and *S. agalactiae*. Bacteroides species and *Clostridium perfringens* were seen in 4 (7%) and 3 (5%) cases, respectively. Only one type of fungal species, *Candida*, was noted as a causative organism, being present in 3 cases (5%) [24,51]. Other bacterial organisms isolated in only a single case included *Edward siellatarda*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Propionibacterium acnes*, *Sphingomonas paucimobilis*, *Pasteurella multocida*, *Citrobacter spp.*, *Fusobacterium necrophorum*, and *Peptostreptococcus tetradius* [20,21,26,27,31,47,52,60,61]. Of note, gram positive cocci (GPC) and gram negative rods (GNR) of unknown species were isolated in 3 (5%) and 4 (7%) cases, respectively [36,42,45,57,66,67,72].

Leukocytosis, defined as an index white blood cell (WBC) count greater than 11,000 cells/ μ L, was also measured and noted in each case

(Table 1). Of the 75 cases reviewed, 5 had no mention of WBC counts, and were listed as 'Unknown/Not Stated' (Table 1). In the remaining 70 cases with WBC counts mentioned, 83% (58/70) demonstrated leukocytosis. Absence of leukocytosis was seen in the remaining 17% of cases (12/70), with one patient carrying a pre-existing diagnosis of HIV and another exhibiting a leukocytopenic picture (WBC < 4000 cells/ μ L). The presence of leukocytosis was noted to be more common in cases associated with pregnancy, seen in 91% of cases (30/33; 3 'Unknown/Not Stated'), compared to 76% of the cases of pyomyoma not associated with pregnancy (28/37; 2 'Unknown/Not Stated').

Blood culture results were mentioned in 63 of the 75 cases reviewed (Table 1). In these 63, 33% (21/63) demonstrated positive blood cultures, with either the causative organism of the pyomyoma isolated, or the presence of one or more of the involved organisms in patients with who had polymicrobial pyomyomas. Negative blood cultures were seen in 67% (42/63) of cases. Blood cultures were noted to be more commonly positive in cases associated with pregnancy, at 39% (12/31; 5 'Unknown/Not Stated'), compared to a positive blood culture rate of 28% in cases not associated with pregnancy (9/32; 7 'Unknown or Not Stated').

All 75 cases reviewed included antibiotic therapy as part of the treatment regimen (Table 1). In 7% of cases (5/75), including our case, antibiotic therapy was the only treatment modality employed. Surgical means were employed as part of treatment in 84% (63/75) of total cases, and included total or subtotal hysterectomy with or without salpingo-oophorectomy (TAH +/- SBO), myomectomy, and surgical or laparoscopic drainage of the pyomyoma. Subtotal or total hysterectomy was performed in 53% (40/75) of cases, with 75% of these hysterectomies including either unilateral or bilateral salpingo-oophorectomy (30/40). This includes a single case of CT-guided drainage, which failed to adequately resolve the patient's condition

[51]. Myomectomy was performed in 25% (19/75) of total cases, including a single case where myomectomy was successfully performed during the 28th week of pregnancy, and followed by a successful cesarean section delivery at 37 weeks gestation [57]. Drainage of the pyomyoma was performed in 11% of total cases (8/75); one case (CT-guided drainage) proceeded to subtotal hysterectomy after treatment failure (Table 1). Of the 8 drainage procedures, 3 were performed surgically (2 open; 1 laparoscopically). The remaining 5 were done via non-surgical means; 3 via CT-guided percutaneous drainage, and 2 using ultrasound-guided percutaneous aspiration and/or drainage methods. Manual removal of the pyomyoma was performed in 4% of cases (3/75); in each case, during examination under anesthesia, the cervical os was noted to be open and a prolapsed pyomyoma protruding from the uterine cavity [12,48,71]. Repair of a fistula was performed in 4 cases; in one as part of the primary treatment following expulsion of the pyomyoma through a para-cervical fistula, and the remaining three as secondary procedures following definitive surgical treatment of the underlying pyomyoma via hysterectomy or myomectomy [12,38,48,71].

A mortality rate of 5.3% (4/75) was noted in the review (Table 1). Between 1945 and 1990, a mortality rate of 25% was observed, with 3 of 12 cases resulting in death. However, since 1990, only one fatality has been reported in 63 cases, resulting in a mortality rate of only 1.6%.

Of the 4 deaths observed, 2 occurred in patients who only received antibiotic therapy as their treatment regimen. One death occurred ~8 hours following a TAH-BSO. The final and most recent death, in 2008, occurred following attempted ultrasound guided percutaneous aspiration and drainage of the pyomyoma; this patient was deemed too ill for surgical treatment and succumbed 53 days after admission [40]. The mortality rates based on treatment modality employed is therefore: 40% for antibiotic therapy alone, 2.5% for hysterectomy with or without salpingo-oophorectomy, 13% for drainage, and 0% for both myomectomy and manual removal of the Pyomyoma (Table 1).

Discussion

In the literature review performed of all 75 cases, just under half of cases with pyomyoma (48%) were associated with pregnancy (Table 1). The patient age in these cases was considerably younger, at 33.1 years of age, as compared to their non-pregnant counterparts, who were on average 15 years older (48.6 y.o.). Post-menopausal patients accounted for just under 1/5th of total cases (19%). Recent delivery, whether vaginally or surgically by cesarean section, was the most common known cause of pyomyoma in our review, confirming previous literature regarding Pyomyoma [30,57,65,70]. Abortions accounted for 26% of total cases of pyomyoma with the majority of these cases involving some type of uterine instrumentation, demonstrating the increased risk of developing pyomyoma with such procedures, which can introduce foreign organisms into the uterine cavity (Table 1). In our case, our patient presented with a septic abortion and underwent subsequent D & C, as is indicated [75]. Uterine instrumentation, however, is itself a risk factor for the development of pyomyoma, and performing a procedure in an already contaminated environment, further increases this risk [6,17,42]. Uterine Artery Embolization (UAE) is a relatively new procedure introduced in the last 30 years as a treatment for

symptomatic leiomyomas as well as adenomyosis, and was implicated in just under ¼ of cases with a known cause [23,25,27,32,68]. Though some amount of pain and fever can be expected following UAE, due to ischemia and degeneration of the fibroid, pyomyoma should be suspected in patients with un resolving fever and abdominal pain following such procedures [23,25,68,72].

Pyomyomas are a relatively rare occurrence, and symptoms are generally non-specific and can masquerade as numerous other intra-abdominal or pelvic pathologies, such as pelvic inflammatory disease, tubo-ovarian abscess, endometritis, gynecological malignancy such as ovarian cancer, intestinal perforation, pyometra, or appendicitis, which can obfuscate an accurate diagnosis [26,30,31,46,57]. Pyomyoma has also been reported to mimic endocarditis [15]. Therefore, a high index of suspicion is required for an accurate patient assessment and diagnosis. Early diagnosis and treatment is absolutely necessary to prevent excessive morbidity and potential mortality. In our review, the most common symptoms in descending order were fever, abdominal and pelvic pain, and complaints of a pelvic or abdominal mass (Figure 2). Less common symptoms included vaginal bleeding or discharge, nausea/vomiting, and weakness or lethargy (Figure 2). These symptoms can encompass a broad differential diagnosis, but should raise suspicion of pyomyoma in patients who have had other more common conditions ruled out, especially those with recent pregnancy and delivery. Pyomyoma should also be highly suspected as a differential diagnosis in patients with the aforementioned presentation when associated with recent uterine instrumentation or UAE, as these procedures have been associated with a high percentage of overall cases.

Numerous imaging modalities can be used to help in establishing the diagnosis of pyomyoma, including pelvic/abdominal ultrasonography, CT-scan, and MRI [32,40,44,49,61,74]. Sonographic findings associated with pyomyoma include enlarged heterogeneously echogenic pelvic mass, presence of mixed solid and cystic components, reverberation artifacts and acoustic shadowing indicating presence of gas, and discontinuity of the uterine wall [26,31,40]. In our patient, heterogeneity of the leiomyoma with mixed solid and cystic components was seen, however signs indicative of the presence of gas were absent. Characteristic CT findings in pyomyoma include presence of gas and debris in the leiomyoma, heterogenous appearance, and thickened fibroid wall with or without rupture [26,40]. Ruptured pyomyoma may also be associated with intraperitoneal free air, ascites, and organized fluid collections [26]. MRI findings include the presence of cystic lesions within the myometrium and the presence of an enhancing peripheral rim [61]. Hemorrhagic and necrotic foci may be seen within the myoma, especially in patients with current or recent pregnancy, and partial or total rupture of the mass may be present as well, similar to findings seen in our patient [61].

Several clinical trials have been proposed to assist in the diagnosis of pyomyoma, the most prominently cited of which includes: Presence of a known leiomyoma, bacteremia or sepsis, and no apparent source of infection [5]. However, in our review, only 33% of reported cases of pyomyoma had the presence of culture positive bacteremia, with the rate being slightly higher in cases associated with pregnancy, at 39%. Presence of bacteremia is therefore not a sensitive finding in the assessment of Pyomyoma. It should also be noted that initiation of antibiotic therapy prior to obtaining blood cultures,

especially regimens including vancomycin, could lead to the presence of falsely negative results, and should be considered when analyzing the significance of such cultures in the diagnostic assessment of these patients [76]. Leukocytosis, however, was determined to be much more sensitive in determining the presence of pyomyoma, observed in 91% of cases associated with pregnancy and 83% of overall cases reviewed (Table 1). Leukocytosis, though a very non-specific finding, can be demonstrably more sensitive when incorporated into the assessment for an infectious etiology such as pyomyoma. C-reactive protein (CRP) levels were not included as part of the characteristics of the 75 cases in our literature review, due to their only recent implementation as an inflammatory marker [79]. CRP is one of the acute-phase proteins that are an early marker of inflammation and/or infection [79]. CRP levels have in the last 20 years been increasingly utilized as potential markers of bacterial infection and sepsis, with a greater sensitivity when compared to leukocytosis, due to the increased prevalence of the latter in many non-infectious inflammatory as well as non-inflammatory conditions [79-82]. Elevated CRP levels were reported in 10 cases, including 7 with negative blood cultures and 1 with normal WBC counts. Procalcitonin (PCT) is a precursor of the hormone calcitonin [24,34,51,57-60,65,70,73], and has been increasingly used as a marker for bacterial infection since its first reported association with bacterial infections, specifically meningitis, in 1993 [80,83]. PCT levels are now routinely performed in many hospitals as part of the laboratory assessment for patients suspected of suffering from bacterial sepsis and septic shock [84]. PCT levels are more expensive and less reproducible than CRP, with many institutions in lesser-developed regions of the world lacking the lab hardware to perform such tests. Many physicians also prefer CRP to PCT levels due to the former's increased reliability in diagnosing sepsis [85]. PCT levels were reported in only 2 cases reviewed, with one case exhibiting negative blood cultures and both demonstrating leukocytosis and elevated CRP levels [60,73]. The significance of CRP and PCT levels with regards to diagnosing pyomyomas is currently not well understood. They can however be the focus of future investigations regarding their utility in predicting and/or indicating the presence of such infective illnesses; especially as their usage becomes increasingly more prevalent in complete diagnostic assessment of such patients.

Causative organisms were isolated in 92% of known cases of pyomyoma, with the majority of these cases being attributed to a single organism. The most commonly isolated organism was *E. coli*. Staphylococcal and streptococcal species were also frequently encountered. Other enteral flora were also encountered in the review as the causative microorganisms, including Enterococcus, Clostridium, Bacteroides, Peptostreptococcus, Proteus, Klebsiella, Actinomyces, and Candida species (Table 1). These findings demonstrate that the gastrointestinal tract can be an important source for pathogens associated with pyomyoma. These organisms can induce infection through a variety of methods, including direct ascension following lower genito-urinary tract infections (which are commonly seen during pregnancy), through direct introduction into the uterine cavity via unsterile urogenital procedures, or due to poor local hygiene [31,33,63,65,70]. Previous literature has demonstrated these organisms gaining access to the uterus and causing the development of pyomyomas through direct invasion from the uterine cavity, spread from adjacent organs such as the colon, or lymphatic and hematogenous spread, all of which were demonstrated in the

review [26,30,31,33,36]. Thorough patient medical and social history should be detailed, however, as unsterile medical or illicit substance IV injection as well as other distant organ system infections were noted as causes in our review [5,18,20,22].

In the treatment of patients with pyomyoma, a combination approach including antibiotics and surgery has most commonly been historically applied. Early surgical intervention has been associated with improved patient morbidity and mortality as well as decreased complication rates [5,19,63,70]. The surgical approach most commonly employed has been hysterectomy with or without salpingo-oophorectomy, seen in 53% of cases we reviewed, and is considered as the gold standard approach to treatment [65,70]. When hysterectomy is performed, the ovaries can be spared in the resection, especially when no involvement of the associated adnexa is present and surrounding pelvic structures are uninvolved, in order to prevent the post-operative development of menopausal symptoms. Myomectomy has been increasingly utilized as the mode of surgical treatment, especially since its first modern use for pyomyoma was reported in 2001 [21]. Myomectomy can therefore be employed as an effective surgical approach in treating patients with pyomyoma, especially those desiring continued fertility, single pyomyoma of small size, and without the presence of any associated complications or adjacent pelvic structure involvement. Myomectomy is also the only effective surgical treatment reported in the management of pregnant patients suffering from pyomyoma, allowing for the preservation of fetal survival and pregnancy until gestation [57]. Patients who undergo surgical pyomyoma removal during pregnancy should have fetal delivery performed via cesarean section due to a very high risk of uterine rupture [57].

More recently, less invasive methods of treatment such as CT-guided drainage have been employed, with moderate success rates, thus allowing patients to avoid undergoing surgery [51]. These methods, however, are not without risk, as failure of these approaches has occurred, and should be managed surgically via either hysterectomy or myomectomy [40,51]. Antibiotic treatment alone, though instituted as the treatment modality in our patient, should not be performed with the intention of sole management. Excluding our patient, only 4 such cases have been reported in the literature, carrying a mortality rate of 50% (Table 1). Surgical procedures have improved in technique and precision over the last 70 years, and can be performed with very high success rates and low patient morbidity & mortality [77]. This is supported by the fact that no fatalities have been reported following surgical management of pyomyomas since 1945.

Mortality rates observed in the review were substantially lower compared to previously reported values of 21-30% [5,46,65] and 15.3% [33]. More recent literature reviews have encompassed an increased number of reported cases, and the most recently reported mortality rate of 6% in 2016 was very similar to the 5.3% rate encountered following our review [70]. Since the first comprehensive literature review was performed on pyomyomas in 1990, a mortality rate of only 1.6% has been observed. This can be attributed to increased utilization of diagnostic imaging modalities such as U/S and CT-scanning, as well as more prompt surgical interventions. With the increased reported incidence of pyomyomas in the last two decades, along with the development of more precise and rapid imaging systems, quicker progression of patient to operative treatment, and

the development of non-invasive definitive management techniques, the mortality rate for pyomyoma should be expected to further decrease with time [77,78].

Conclusion

Pyomyoma is a rare complication of leiomyoma seen in only 75 patients since 1945. Almost half of cases are associated with pregnancy, and just under ¼ are post-menopausal. History of abortion and uterine instrumentation are common causes of pyomyoma, and UAE has been recognized as an evolving cause, especially with increasing performance of this procedure. Patients commonly present with fever, abdominal or pelvic pain, complaints pelvic or abdominal mass, nausea/vomiting, and vaginal discharge or bleeding. The majority of cases are a single organism infection in nature, with *E. coli* being the most commonly isolated organism. Many other microorganisms isolated are associated with human enteral and skin colonization, and can represent a possible source of infection, similar to what is observed in other lower uro-genital tract infections. Blood cultures, when reported, were positive in only one-third of cases, and thus are not reliable in helping to isolate a causative organism in order to tailor anti-microbial treatment, or to establish a diagnosis. Leukocytosis is a more reliable indicator of infection in pyomyoma, being present in 83% of known cases. Leukocytosis is also more common in pyomyoma associated with pregnancy, being reported in 91% of such cases, and can, along with the presence of fever, potentially replace bacteremia within the triad of pyomyoma. The utility of CRP or PCT levels were not studied, but could be of potential prognostic use; further analysis is required before recommendations can be made. Multiple treatment modalities exist, all of which incorporate antibiotic coverage. The most commonly instituted therapy consists of hysterectomy, total or subtotals, with or without salpingo-oophorectomy, and is considered the gold standard in management of pyomyoma. Myomectomy however, is becoming increasingly more common as a treatment modality, and is the only established treatment that allows for fetal survival when pyomyoma occurs during pregnancy. Imaging-guided drainage methods, using U/S and CT, have also been recently performed with some success; however failure rates can be high, necessitating definitive surgical treatment. Mortality rates in the review are currently at 5.3%, with rates since 1990 at 1.8%. As clinical knowledge and understanding of pyomyoma presentation and treatment evolves, earlier diagnosis and treatment are expected to be employed resulting in mortality rates further declining.

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Disclosure of Interests

The authors declare no conflicts of interest regarding the publication of this paper

Contribution to Authorship

O. Azimi-Ghomi authored the case report and researched the topic of pyomyoma, sourced the referenced articles involved in the literature review, recorded the data, constructed the tables and percentage calculations, and authored the final article. A. Mayrer

and J Gradon were involved in the selection of the review and study characteristics, and assisted in editing the manuscript.

Details of Ethics Approval

Patient consent for publishing of the case report was obtained. No other ethics approval or consent was required due to the context of the article consisting of a retrospective literature review.

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