



# Management of lumbar spondylodiscitis developing after laparoscopic sacrohysteropexy with a mesh

# A case report and review of the literature

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## **Abstract**

**Introduction:** Lumbar spondylodiscitis is a rare and severe complication of laparoscopic sacrohysteropexy with a polypropylene mesh. However, a case of lumbar spondylodiscitis following laparoscopic sacrohysteropexy has not been reported so far. We present a case of lumbar spondylodiscitis following laparoscopic sacrohysteropexy with a mesh. We also discuss 33 cases of lumbar spondylodiscitis following sacral colpopexy and (or) rectopexy with a mesh.

**Patient concerns:** A 46-year-old woman with 3 previous vaginal deliveries underwent laparoscopic mesh sacrohysteropexy for stage III uterine prolapse. One month after surgery, the patient developed persistent symptoms, such as stiffness of the lumbosacral portion, low back pain (LBP), persistent swelling, pain between the right iliac crest and the buttock, inability to bend down, and pain in the right lower limb. Symptoms were alleviated by a nonsteroidal anti-inflammatory drug. However, in the last 7 days, symptoms worsened and she was unable to stand or walk. The patient had very limited leg mobility.

**Diagnosis:** Blood routine examination, erythrocyte sedimentation rate, C-reactive protein, and magnetic resonance imaging (MRI) of the lumbar spine indicated lumbar pyogenic spondylodiscitis.

**Interventions:** Removal of mesh and hysterectomy via laparoscopy were performed immediately, and antibiotics were given simultaneously. However, on the basis of MRI findings and persistent symptoms, debridement, laminectomy, spinal canal decompression, bone grafting, and internal fixation via pedicle screw placement were performed 5 months after laparoscopic sacrohysteropexy.

**Outcomes:** All symptoms were alleviated 5 days after the operation. The patient could stand in the erect position and raise her lower limbs within 2 weeks. She could resume her normal activities within 2 months after the operation, and her X-ray appeared normal

**Conclusion:** Persistent LBP and radiating pain may be the signals of lumbar spondylodiscitis. MRI is the gold standard diagnostic examination for lumbar spondylodiscitis. Awareness of symptoms, such as LBP and radiating pain symptoms, timely diagnosis, mesh removal, and referral to orthopedists are important to prevent more severe complications. Surgical practice needs to be improved further and any other infections should be treated immediately as the most likely causes of lumbar spondylodiscitis are related to the mesh and other infections.

**Abbreviations:** CT = computed tomography, LBP = low back pain, MRI = magnetic resonance imaging.

Keywords: lumbar spondylodiscitis, sacral colpopexy, sacral rectopexy, sacrohysteropexy

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This study was approved by the ethics committee of the Affiliated Hospital of North Sichuan Medical College. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

The datasets generated and analyzed during the present study are available from the corresponding author on reasonable request.

The authors have no conflicts of interest to disclose.

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# 1. Introduction

Laparoscopic sacrohysteropexy with a mesh is a variation of the sacral colpopexy to correct apical prolapse in women who desire uterine preservation.<sup>[1]</sup>

Spondylodiscitis, also referred to as pyogenic discitis and vertebral osteomyelitis, is defined as an infection limited to the intervertebral disc (discitis) and the adjacent vertebrae (vertebral osteomyelitis). Spondylodiscitis is a condition that includes a spectrum of spinal infections such as discitis, osteomyelitis, epidural abscess, meningitis, subdural empyema, and spinal cord abscess. Awareness of symptoms, timely diagnosis, and multidisciplinary approach to the management of this condition are important to prevent other severe complications. [4]

We present a case of lumbar spondylodiscitis following laparoscopic sacrohysteropexy with a mesh that was referred to orthopedists for surgery. We also evaluate the current literature to understand how to manage lumbar spondylodiscitis developing after laparoscopic sacrohysteropexy with a mesh.

# 2. Case report

A 46-year-old woman with 3 previous vaginal deliveries suffered from stage III uterine prolapse for 1 year and it had worsened during the last 6 months. Five months ago, laparoscopic sacrohysteropexy was performed using a Yshaped polypropylene mesh. A prophylactic antibiotic was used within 24 hours in the absence of infection. Her past medical history was unremarkable. After the procedure, the pelvic organ prolapse disappeared. One month after surgery, the patient developed discomfort in the lumbosacral portion that continuously persisted for 4 months. The symptoms included stiffness of the lumbosacral portion, low back pain (LBP), persistent swelling, pain between the right iliac crest and the buttock, inability to bend down, and pain in the right lower limb. Symptoms were alleviated after a nonsteroidal antiinflammatory drug was prescribed in the outpatient clinic. But in the last 7 days, symptoms were not alleviated and they worsened, and the patient was unable to stand or walk. The legs could only be moved away from the bed up to 20 cm because of pain. Primitive reflexes were negative and there was no loss of sensory function. Then the patient was referred for admission. Blood routine examination, erythrocyte sedimentation rate, C-reactive protein, and magnetic resonance imaging (MRI) of the lumbar spine indicated lumbar pyogenic spondylodiscitis (Fig. 1). Y-shaped polypropylene mesh was removed and hysterectomy was conducted via laparoscopy immediately, and antibiotics were given simultaneously. During the operation, a festering wound was seen at the location of the stitches over the lumbosacral portion and the mesh suture was placed higher than its usual level. Escherichia coli bacteria were found at the location of the stitches. Tienam was given for 2 weeks as E coli bacteria are sensitive to this drug. The patient was referred to orthopedists because of persistent symptoms. MRI indicated bony destruction of the lower part of the L5 vertebra and the dome of the sacrum and absence of favorable evolution (Fig. 2). Through the retroperitoneal lumbar approach, destruction of the vertebral body between the fifth lumbar vertebra and the first sacral vertebra was seen, and degeneration of the intervertebral disc and necrosis of the lumina of the L5 vertebra were also seen. Debridement, laminectomy, spinal canal decompression, bone grafting, and



Figure 1. MRI: Lumbar pyogenic spondylodiscitis, enhancement of soft tissues surrounding the L5-S1 vertebrae (arrow). MRI = magnetic resonance imaging.

internal fixation via pedicle screw placement were conducted 5 months after laparoscopic sacrohysteropexy. Symptoms were alleviated 5 days after the operation, and the pain decreased. The patient was discharged on the seventh day after the operation. The patient was able to stand in the erect position and raise her lower limbs within 2 weeks. The patient returned to normal activity within 2 months after the operation, and the X-ray also appeared normal (Fig. 3).



Figure 2. MRI after mesh removal 2 wk later: bony destruction of the lower part of the L5 vertebra and the dome of the sacrum (arrow). MRI = magnetic resonance imaging.



Figure 3. Lumbar vertebral X-ray: normal findings (arrow).

#### 3. Discussion

Laparoscopic sacrohysteropexy with a mesh is considered to be the gold standard for apical prolapse in young women who desire uterine preservation. [1] Mesh graft can lead to infections and graft rejection, and different conditions require different management therapies. [5] Lumbar spondylodiscitis is a rare and severe complication, which can cause LBP, fever, and radiating pain symptoms, such as pain in the buttock and leg, and even mobility limitation. [6] A case of lumbar spondylodiscitis following laparoscopic sacrohysteropexy has not been reported so far. Only cases of lumbar spondylodiscitis following sacral colpopexy and (or) rectopexy with a mesh have been reported.

We performed a literature search via PubMed, and we found 33 cases of lumbar spondylodiscitis following sacral colpopexy and (or) rectopexy with a mesh (Table 1). Summary of the characteristics is presented in Table 2. Thirty-four women with a median age of 60 years (range, 42-80 years) were diagnosed with spondylodiscitis following sacrohysteropexy, sacral colpopexy, and (or) rectopexy with a mesh. They visited their doctors with symptoms. The median time to symptom presentation was 14 months, and it ranged from 6 days to 8 years. LBP occurred in every case. Further, 38% of the patients suffered from fever and 35% of the patients suffered from radiating pain symptoms, which mostly predicted the need for referral to orthopedists for surgical interventions (Table 3). Regardless of the recovery time after surgery, the possibility of spondylodiscitis must be considered when the patients present with LBP, fever, and especially radiating pain symptoms, which may predict the presence of severe spondylodiscitis requiring multidisciplinary surgical interventions.

MRI can indicate the early stage of spondylodiscitis reflecting the obvious imaging changes. In our study, 97% of cases of spondylodiscitis were diagnosed by MRI; excluding 1 case that was diagnosed by computed tomography (CT) and MRI was not

Cases of spor	ndylod	Cases of spondylodiscitis following sacrohysteropexy, sacral colpopexy, and rectopexy with a mesh.	ohysteropexy, sacra	dodloo l	exy, and rectopexy	with a mesh.			
Author, yr	Age	Prolapse procedure	Main symptoms and time to presentation	Fever	Symptom relief and time	Diagnostic tools indicating spondylodiscitis	Pathogens	Managements	Possible causes
Case	46	Laparoscopic sacrohystero- pexy	LBP Radiating to legs for 1 mo	<b>8</b>	Full recovery at 2 mo	MRI	Local tissue: Escherichia coli	Laparoscopic mesh removal and hysterectomy  Debridement, laminectomy spinal, canal decompression, bone graft Internal fixation of pedicle screw placement  Anthiorics iv	Suture placement higher the of level of the sacra promontory
Boyd, <sup>[7]</sup> 2018	71	Robotic sacrocolpopexy	LBP for 6 wk	Yes	Doing well, (12 mo) intermittent LBP	CT/MRI	Local tissue: Candida albicans	Laparoscopic removal of the mesh Antimicrobial treatment (oral fluconazole for 12 mo)	Suture placement 2 cm above the sacral promon tory, higher than the usus
Ugurl-ucan, <sup>[6]</sup> 2018	52	Total laparoscopic hysterect- omy and sacrocolpopexy	LBP 3 wk	% 8	Full recovery at 12 mo	MRI	Negative	Laparoscopic mesh excision Ab for 4 wk	Not noted
Nunez-Pereira S, <sup>[8]</sup> 2016	80	Abdominal sacrocolpopexy	LBP Radiating leg pain for 7 yr	Yes	Full recovery at 6 wk	MRI	Enterococcus faecalis	Debridement and stabilization with transforaminal lumbar interbody fusion.  Removal of the mesh Removal of the rectal fishula and protective ileostomy Ab for 6 wk	Rectal fistula following me penetration
Jenson, <sup>(9)</sup> 2016	29	Laparoscopic sacral colpopexy	LBP for 4 mo	<u>8</u>	Full recovery at 4 mo	MRI	Local culture: Entero- coccus faecalis, vanco- mycin-resistant Entero- coccus gallinarum, and Barhamiles faarilis	Laparoscopic mesh Removal Ab for 12 wk	Vaginal mesh erosion
Murat Api, <sup>[5]</sup> 2015	53			Yes		MRI	negative		Not noted

m onsual

Author, yr	Age	Prolapse procedure	Main symptoms and time to presentation	Fever	Symptom relief and time	Diagnostic tools indicating spondylodiscitis	Pathogens	Managements	Possible causes
		Total hysterectomy with sacral colpopexy via laparoscopy	LBP Radiating pain to the upper thighs for 6 d		Full recovery immedi- ately following mesh removal			Excision of mesh via laparoscopy on post- operative 52nd d Ab	
	92	Total hysterectomy with sacral colpopexy via laparot-	LBP Radiating pain to the upper thighs for 53	Yes	Full recovery immediately following mesh	MRI	Negative	Excision of the mesh via laparotomy on post-operative 58 <sup>th</sup> d Ab	Not noted
Brito, <sup>[10]</sup> 2015	61	Subtotal laparoscopic hysterectomy and sacrocolpo-	LBP for 12 d	Yes	Full recovery at 10 wk	MRI	Staphylococcus aureus	Mesh removal Ab for 6 wk.	Not noted Breast cancer
Tymchak, <sup>[11]</sup> 2015	61	Transvaginal hysterectomy with abdominalsacrocolpo-	LBP 1 mo	No	Full recovery	MRI	Negative	Mesh removal Abdominal Ab in for 6 and 2 and 2 and 2	Not noted
Vujovic, <sup>[12]</sup> 2015	20	Laparoscopic ventral mesh	LBP for 11 wk	% 8	Full recovery at 3 mo	CT/MRI	Blood culture: negative	Ab it it is what it is who stated that the strew removal Ab for 3 more mo.	Not noted
Apostolis <sup>[13]</sup> 2014	99	Laparoscopic supracervical hysterectomy and sacrocolpopexy	LBP for one and a half wk	Yes	Full recovery at 6 wk after mesh removal	MRI	Blood culture: Ingarive Blood culture: Bacter- oides fragilis bactere- mia Mesh: Enterohacter	Laminectomy and debridement of the epidural phlegmon Antibiotics for 5 wk	Past history of dental extraction of infected teeth.
Anand, <sup>[14]</sup> 2014	70	Robotic supracervical hysterectomy with sacrocolpopexy	LBP Radiating leg pain for 3 mo	Yes	Full recovery at 12 mo	CTMRI	Blood culture: negative Vertebral spine culture	Mesh removal Anterior LESS1 Discectomy and sharp debridement of the	Recurrent UTI
Propst, <sup>(4)</sup> 2014	99	Robotic-assisted laparo- scopic sacral colpopexy, ventral rectopexy	LBP Radiating bilateral leg pain for 8 wk	<u>8</u>	Full recovery at 18 mo	MRI	Blood culture negative Epidural culture: <i>Bac-</i> <i>teroides fragilis</i>	Antifungal antibiotics for 12 wk Right hemilaminectorny of L4 and L5 with removal of the epidural phlegmon and decompression of the S1 nerve root After 3 wk Laparotorny mesh removal and anterior L5-S1 discectorny and debride- ment.	The location of the mesh was above the S1 vertebra and not within the disc space
	55	Total abdominal hysterect- omy and sacral colpopexy	LBP Limitied mobility for 3 yr	N N	Not reported	CI	Prevotella, Bacteroides and Streptococcus viri- dans	Ab for 6 wk Mesh excision because of mesh erosion at 2 yr postoperatively Removal of the abscess Ah iv.	Mesh erosion at the vaginal apex
Grimes, <sup>[15]</sup> 2012	63	Sacral colpopexy	LBP Radiating to the buttock for 4 mo	ON.	Full recovery at 11 mo	CT and MRI	Local tissue: C albicans	surgical debridement with mesh removal and tissue excision in the surgical plane 2 discectomies, L5 corpectomy, partial corpectomies, canal decompression, strut fusion, and posterior screw and rod stabilization and fusion.	Yeast vaginitis
Vоеlkar, <sup>116]</sup> 2012	28	Sacral colpopexy	LBP for 3 yr	Yes	Full recovery at 3 mo	MBI	Local tissue: Proteus mirabilis, Morganella morganii, Sta- phytococcus warneri, and Enterococus fae- calis	Au Violo Ward of all to 3 file Above the Automotal of the neovagina, debridement of the intected tissue, and existion of the intervertebral disc at LS/S1 with replacement through a bone graft second surgical session dorsal instrumentation of the segments L5 and S1	Not noted Malignant melanoma of the vagina
Rajamaheswari, <sup>[17]</sup> 2012	42	Abdominal hysterectomy and sacrocolpopexy	m PE	N N	Full recovery at 6 mo	MRI	Not reported	Ab for 3 mo removal of the mesh by laparotomy Ab oral for 4 wk	Mesh erosion
Roth, <sup>[18]</sup> 2012	92	Laparoscopic sacral colpo- pexy	LBP for 7 yr	% 8	Full recovery at 4 mo	MRI	Local tissue: Streptococcus viridans	Laparoscopic enterolysis, drainage of the abscess, and explantation of the remaining	Mesh erosion

Author, yr	Age	Prolapse procedure	Main symptoms and time to presentation	Fever	Symptom relief and time	Diagnostic tools indicating spondylodiscitis	Pathogens	Managements	Possible causes
Draaisma, <sup>I19]</sup> 2011	45	Laparoscopic sacral ventral rectopexy	LBP radiating to both legs for 1 mo	Yes	Full recovery at 7 wk	MRI	and <i>Streptococcus</i> intermedius.	mesh. Ab Iv for 4 wk Mesh removal Ab Iv for 7 wk	Not noted systemic lupus enythematosus using hydro-
	22	Laparoscopic ventral sacral	LBP for 2 mo	Yes	Full recovery at 8 wk	MRI	Not reported	Ab IV for 4 wk and oral for 4 wk	xycnioroquine Not noted
Collins, <sup>[20]</sup> 2011	74	recubexy Abdominal sacral colpopexy	Chronic back pain for 8 yr	No	Full recovery at 2 mo	MRI	Blood culture: Bacter- oides Local: fragilis. vanco- mycin resistant entero-	Mesh removal Ab debridement	Б
Muffly, <sup>[21]</sup> 2010	46	Transvaginal mesh followed by robot-assisted sacral colpopexy	LBP for 1 yr	N	Full recovery at 3 mo	MRI	coocus Blood: negative Local tissue: coagu- lase-negative Staphylo-	Discectomy, sacral debridement, and mesh removal Ab IV for 7 wk	Vaginitis diabetes mellitus
Nosseir, <sup>[22]</sup> 2010	22	Sacral colpopexy	LBP for 6 wk	No No	Full recovery at 6 mo	MRI	Local tissue:	Ab iv for 8 wk	Not noted
Downing, <sup>[23]</sup> 2008	52	Laparoscopic uterus-preser- ving cervicosacropexy	LBP radiating to the hip and leg for 14 mo	9N	continued to have back pain	MRI	Staphrylococcus Local tissue: Staphylococcus aureus	Total abdominal hysterectomy, and excision of an infected mesh	Vaginal mesh erosion
Taylor, <sup>[24]</sup> 2006	64	Laparoscopic-assisted vagi- nal hysterectomy, sacral col-	LBP for 14 mo	Not reported	Not reported	MRI	Blood and bone cultures: <i>S aureus</i>	Ab iv, mesh removal, and decompression laminectomy	Vaginal mesh erosion
Hart, <sup>[25]</sup> 2004	42	popexy Total abdominal hysterect- omy, abdominal sacral col- popexy,	LBP weakness in the lower extremities for 5 mo	Yes	Full recovery at 6 mo	MRI	Negative	transvaginal mesh removal Extensive debridement of necrotic sacral periosteum Ah iv for A wide	Vaginal mesh erosion
Salman, <sup>[26]</sup> 2003	29	Sacrocolpopexy	LBP, radiating to both	N <sub>o</sub>	Full recovery at 3 mo	MRI	Not reported	Debridement and stabilization with screws	Not noted
Beloosesky, [27] 2002	74	Abdominal colposacropexy	LBP for 7 wk	Yes	Full recovery at 3 mo	CT/MRI	Local tissue: Staphylo-	Ab iv for 3 mo	En
Kapoor, <sup>[28]</sup> 2002	63	Laparascopic sacrocolpo- pexy	LBP for 3 wk	Yes	Full recovery at 8 wk	MRI	Blood culture: beta haemolytic streptococ-	Ab IV for 8 WK Ab IV for 8 WK	Wound infection at one of the port sites
Cosson, <sup>[29]</sup> 2001	45	Laparoscopic sacropexy	LBP for 2 yr	N N	Full recovery	MRI	Local CT-guide aspi- rate: F-mli	Ab iv for 3 wk Mesh removal Ah iv for 8 wk	Б
Weidner, <sup>[30]</sup> 1997	29	Abdominal sacral colpopexy	LBP for 5 yr	No	Not reported	MRI	Blood: Blood: Negative Local CT-guided aspirate	Ab IV for 4 wk	Not noted
	26	Total abdominal hysterect- omy, sacral colpopexy	LBP for 4 mo	N N	Full recovery	MRI	P aeruginosa Both cultures (blood and local aspirate): S wiridans & fractilis	CT-guided drainage Ab IV for 12 wk	Not noted
Cranney, <sup>[31]</sup> 1994	72	Abdominal-vaginal sacral colpopexy	LBP for 4 wk	Yes	Full recovery at 6 wk	MRI	Blood culture: positive Local tissue: positive	Debridement of the mesh and Lumbar vertebrae, discectomy, and spinal fusion Ah in for 6 wild	Б
Cailleux, <sup>[32]</sup> 1991	54	Abdominal supracervical hysterectomy and sacral	LBP for 1.5 mo	Yes	Full recovery at 3 mo	MRI	Blood and tissue culture: <i>E coli</i>	Mesh Removal Ab Iv for 3 mo	Postoperative pelvic abscess

Ab=antibiotics, CT = computed tomography, LBP = low back pain, MRI = magnetic resonance imaging, UTI = urinary tract infection.

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## Table 2

Summary of the characteristics of cases of spondylodiscitis following sacrohysteropexy, sacral colpopexy, and rectopexy with a mesh (including the presented case and 33 cases from literature review).

Characteristic	Data
Age in yr, median (range)	60 (42–80)
Prolapse procedure, n (%)	Open Abdominal sacral colpopexy (ASC), 15 (44) Laparoscopic ASC, 14 (41) Robotic ASC, 4 (12)
Main symptoms, n (%)	Laparoscopic sacrohysteropexy, 1 (3) Low back pain (LBP), 34 (100) Radiating pain symptoms, 12 (35) Fever, 13 (38)
Time to presentation, median (range)	14 mo (6 d–8 yr)
Detection tools, n (%)	MRI, 33 (97) CT, 1 (3) MRI and CT, 6 (18)
Recovery, n (%)	Full recovery, 30 (88) Continuous LBP, 2 (6) Not reported, 2 (6)
Culture (blood culture and tissue culture), n (%)	Local culture, 24 (71) Blood culture, 7 (21) Both blood and local culture, 6 (18)
Possible causes, n (%)	Related to the mesh, 11 (32) Placement at a higher level than the sacral promontory, 3 (9) Vaginal mesh erosion, 8 (24)
	Rectal fistula following mesh penetration, 1 (3) Related infection, 10 (29) UTI, 5 (15)
	Vaginitis, 2 (6) Post-operative pelvic abscess, 1 (3) Wound infection at one of the port sites, 1 (3) Dental extraction of infected teeth, 1 (3)
Management, n (%)	Not noted, 13 (38)  Antibiotics alone, 4 (12)  Surgical intervention, 30 (88)  Mesh removal, 24 (71)
	(excluding 1 case of mesh removal because of mesh erosion)  Referral to orthopedists for surgical intervention, 15 (44)

 ${\tt CT} \! = \! {\tt computed tomography}, \ {\tt MRI} \! = \! {\tt magnetic resonance imaging}, \ {\tt UTI} \! = \! {\tt urinary tract infection}.$ 

conducted. CT-guided aspiration can sometimes be useful for diagnosing local infection.

Seventy-one percent of the patients developed local pathogen infection, which included bacterial and fungal infections. It was only infection, and not graft rejection. [5] CT-guided aspiration can sometimes be useful for diagnosing local infection and for prescribing the correct drugs.

# Table 3

The relationship between occurrence of radiating pain symptoms and referral to orthopedists.

	Referral to	orthopedists	
Radiating pain symptoms	Presence	Absence	P
Presence	8	4	.000
Absence	8	14	

Antibiotics alone were effective in only 4 cases, that is, 12% of the total cases; thus, showing a low percentage. Most of the patients needed surgical interventions. Mesh removal and debridement were effective in majority of the cases, while 44% of the cases needed multidisciplinary surgical interventions, mainly orthopedic surgery. Further, 88% of the patients were able to return to normal daily activity, and only 6% of the patients suffered from intermittent LBP.

The possible causes of lumbar spondylodiscitis were mainly related to the mesh (32%) and other infections (29%), while the other causes of lumbar spondylodiscitis were not noted. Meshrelated causes included vaginal mesh erosion (24%), including mesh penetration into the rectum in 1 case, and suture placement at a level higher than the usual placement level (9%). Other infections included urinary tract infection in 5 cases (15%), vaginitis in 2 cases (6%), postoperative pelvic abscess in 1 case (3%), wound infection at 1 of the port sites in 1 case (3%), and dental extraction of infected teeth in 1 case (3%). Surgical practice needs to be improved further and any other infections should be treated immediately.

In conclusion, persistent LBP and radiating pain may be the signals of lumbar spondylodiscitis. MRI is the gold standard diagnostic examination for lumbar spondylodiscitis. Awareness of symptoms, especially LBP, fever, and radiating pain symptoms, and timely MRI of the lumbar spine can help the early diagnosis of spondylodiscitis. Local bacterial culture can be useful for prescribing more effective antibiotics. Mesh removal and debridement are the main gynecological surgical interventions. Timely referral to orthopedists can prevent additional surgeries.

#### **Author contributions**

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Software: Da-Cheng Qu. Supervision: Hong-Gui Zhou. Validation: Hong-Gui Zhou.

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